

Figure 29 shows a nucleotide sequence (SEQ ID NO:51) of a native sequence PRO1411 (UNQ729) cDNA, wherein SEQ ID NO:51 is a clone designated herein as "DNA59212-1627". The start and stop codons are shown in bold and underlined font.

Figure 30 shows the amino acid sequence (SEQ ID NO:52) derived from the coding sequence of SEQ ID NO:51 shown in Figure 29.

5 Figure 31 shows a nucleotide sequence (SEQ ID NO:53) of a native sequence PRO1295 (UNQ664) cDNA, wherein SEQ ID NO:53 is a clone designated herein as "DNA59218-1559". The start and stop codons are shown in bold and underlined font.

Figure 32 shows the amino acid sequence (SEQ ID NO:54) derived from the coding sequence of SEQ ID NO:53 shown in Figure 31.

10 Figure 33 shows a nucleotide sequence (SEQ ID NO:55) of a native sequence PRO1359 (UNQ708) cDNA, wherein SEQ ID NO:55 is a clone designated herein as "DNA59219-1613". The start and stop codons are shown in bold and underlined font.

Figure 34 shows the amino acid sequence (SEQ ID NO:56) derived from the coding sequence of SEQ ID NO:55 shown in Figure 33.

15 Figure 35 shows a nucleotide sequence (SEQ ID NO:57) of a native sequence PRO1190 (UNQ604) cDNA, wherein SEQ ID NO:57 is a clone designated herein as "DNA59586-1520". The start and stop codons are shown in bold and underlined font.

Figure 36 shows the amino acid sequence (SEQ ID NO:58) derived from the coding sequence of SEQ ID NO:57 shown in Figure 35.

20 Figure 37 shows a nucleotide sequence (SEQ ID NO:62) of a native sequence PRO1772 (UNQ834) cDNA, wherein SEQ ID NO:62 is a clone designated herein as "DNA59817-1703". The start and stop codons are shown in bold and underlined font.

Figure 38 shows the amino acid sequence (SEQ ID NO:63) derived from the coding sequence of SEQ ID NO:62 shown in Figure 37.

25 Figure 39 shows a nucleotide sequence (SEQ ID NO:67) of a native sequence PRO1248 (UNQ631) cDNA, wherein SEQ ID NO:67 is a clone designated herein as "DNA60278-1530". The start and stop codons are shown in bold and underlined font.

Figure 40 shows the amino acid sequence (SEQ ID NO:68) derived from the coding sequence of SEQ ID NO:67 shown in Figure 39.

30 Figure 41 shows a nucleotide sequence (SEQ ID NO:69) of a native sequence PRO1316 (UNQ682) cDNA, wherein SEQ ID NO:69 is a clone designated herein as "DNA60608-1577". The start and stop codons are shown in bold and underlined font.

Figure 42 shows the amino acid sequence (SEQ ID NO:70) derived from the coding sequence of SEQ ID NO:69 shown in Figure 41.

35 Figure 43 shows a nucleotide sequence (SEQ ID NO:71) of a native sequence PRO1197 (UNQ610) cDNA, wherein SEQ ID NO:71 is a clone designated herein as "DNA60611-1524". The start and stop codons are shown in bold and underlined font.

Figure 44 shows the amino acid sequence (SEQ ID NO:72) derived from the coding sequence of SEQ ID NO:71 shown in Figure 43.

Figure 45 shows a nucleotide sequence (SEQ ID NO:76) of a native sequence PRO1293 (UNQ662) cDNA, wherein SEQ ID NO:76 is a clone designated herein as "DNA60618-1557". The start and stop codons are shown in bold and underlined font.

5 Figure 46 shows the amino acid sequence (SEQ ID NO:77) derived from the coding sequence of SEQ ID NO:76 shown in Figure 45.

Figure 47 shows a nucleotide sequence (SEQ ID NO:78) of a native sequence PRO1380 (UNQ717) cDNA, wherein SEQ ID NO:78 is a clone designated herein as "DNA60740-1615". The start and stop codons are shown in bold and underlined font.

10 Figure 48 shows the amino acid sequence (SEQ ID NO:79) derived from the coding sequence of SEQ ID NO:78 shown in Figure 47.

Figure 49 shows a nucleotide sequence (SEQ ID NO:83) of a native sequence PRO1265 (UNQ636) cDNA, wherein SEQ ID NO:83 is a clone designated herein as "DNA60764-1533". The start and stop codons are shown in bold and underlined font.

15 Figure 50 shows the amino acid sequence (SEQ ID NO:84) derived from the coding sequence of SEQ ID NO:83 shown in Figure 49.

Figure 51 shows a nucleotide sequence (SEQ ID NO:85) of a native sequence PRO1250 (UNQ633) cDNA, wherein SEQ ID NO:85 is a clone designated herein as "DNA60775-1532". The start and stop codons are shown in bold and underlined font.

20 Figure 52 shows the amino acid sequence (SEQ ID NO:86) derived from the coding sequence of SEQ ID NO:85 shown in Figure 51.

Figure 53 shows a nucleotide sequence (SEQ ID NO:87) of a native sequence PRO1475 (UNQ746) cDNA, wherein SEQ ID NO:87 is a clone designated herein as "DNA61185-1646". The start and stop codons are shown in bold and underlined font.

25 Figure 54 shows the amino acid sequence (SEQ ID NO:88) derived from the coding sequence of SEQ ID NO:87 shown in Figure 53.

Figure 55 shows a nucleotide sequence (SEQ ID NO:94) of a native sequence PRO1377 (UNQ714) cDNA, wherein SEQ ID NO:94 is a clone designated herein as "DNA61608-1606". The start and stop codons are shown in bold and underlined font.

30 Figure 56 shows the amino acid sequence (SEQ ID NO:95) derived from the coding sequence of SEQ ID NO:94 shown in Figure 55.

Figure 57 shows a nucleotide sequence (SEQ ID NO:99) of a native sequence PRO1326 (UNQ686) cDNA, wherein SEQ ID NO:99 is a clone designated herein as "DNA62808-1582". The start and stop codons are shown in bold and underlined font.

35 Figure 58 shows the amino acid sequence (SEQ ID NO:100) derived from the coding sequence of SEQ ID NO:99 shown in Figure 57.

Figure 59 shows a nucleotide sequence (SEQ ID NO:101) of a native sequence PRO1249 (UNQ632) cDNA, wherein SEQ ID NO:101 is a clone designated herein as "DNA62809-1531". The start and stop codons are shown in bold and underlined font.

Figure 60 shows the amino acid sequence (SEQ ID NO:102) derived from the coding sequence of SEQ ID NO:100 shown in Figure 59.

5 Figure 61 shows a nucleotide sequence (SEQ ID NO:103) of a native sequence PRO1315 (UNQ681) cDNA, wherein SEQ ID NO:103 is a clone designated herein as "DNA62815-1578". The start and stop codons are shown in bold and underlined font.

Figure 62 shows the amino acid sequence (SEQ ID NO:104) derived from the coding sequence of SEQ ID NO:103 shown in Figure 61.

10 Figure 63 shows a nucleotide sequence (SEQ ID NO:110) of a native sequence PRO1549 (UNQ782) cDNA, wherein SEQ ID NO:110 is a clone designated herein as "DNA62845-1684". The start and stop codons are shown in bold and underlined font.

Figure 64 shows the amino acid sequence (SEQ ID NO:111) derived from the coding sequence of SEQ ID NO:110 shown in Figure 63.

15 Figure 65 shows a nucleotide sequence (SEQ ID NO:115) of a native sequence PRO1430 (UNQ736) cDNA, wherein SEQ ID NO:115 is a clone designated herein as "DNA64842-1632". The start and stop codons are shown in bold and underlined font.

Figure 66 shows the amino acid sequence (SEQ ID NO:116) derived from the coding sequence of SEQ ID NO:115 shown in Figure 65.

20 Figure 67 shows a nucleotide sequence (SEQ ID NO:117) of a native sequence PRO1374 (UNQ711) cDNA, wherein SEQ ID NO:117 is a clone designated herein as "DNA64849-1604". The start and stop codons are shown in bold and underlined font.

Figure 68 shows the amino acid sequence (SEQ ID NO:118) derived from the coding sequence of SEQ ID NO:117 shown in Figure 67.

25 Figure 69 shows a nucleotide sequence (SEQ ID NO:122) of a native sequence PRO1311 (UNQ677) cDNA, wherein SEQ ID NO:122 is a clone designated herein as "DNA64863-1573". The start and stop codons are shown in bold and underlined font.

Figure 70 shows the amino acid sequence (SEQ ID NO:123) derived from the coding sequence of SEQ ID NO:122 shown in Figure 69.

30 Figure 71 shows a nucleotide sequence (SEQ ID NO:127) of a native sequence PRO1357 (UNQ706) cDNA, wherein SEQ ID NO:127 is a clone designated herein as "DNA64881-1602". The start and stop codons are shown in bold and underlined font.

Figure 72 shows the amino acid sequence (SEQ ID NO:128) derived from the coding sequence of SEQ ID NO:127 shown in Figure 71.

35 Figure 73 shows a nucleotide sequence (SEQ ID NO:129) of a native sequence PRO1244 (UNQ628) cDNA, wherein SEQ ID NO:129 is a clone designated herein as "DNA64883-1526". The start and stop codons are shown in bold and underlined font.

Figure 74 shows the amino acid sequence (SEQ ID NO:130) derived from the coding sequence of SEQ ID NO:129 shown in Figure 73.

Figure 75 shows a nucleotide sequence (SEQ ID NO:131) of a native sequence PRO1246 (UNQ630) cDNA, wherein SEQ ID NO:131 is a clone designated herein as "DNA64885-1529". The start and stop codons are shown in bold and underlined font.

5 Figure 76 shows the amino acid sequence (SEQ ID NO:132) derived from the coding sequence of SEQ ID NO:131 shown in Figure 75.

Figure 77 shows a nucleotide sequence (SEQ ID NO:133) of a native sequence PRO1356 (UNQ705) cDNA, wherein SEQ ID NO:133 is a clone designated herein as "DNA64886-1601". The start and stop codons are shown in bold and underlined font.

10 Figure 78 shows the amino acid sequence (SEQ ID NO:134) derived from the coding sequence of SEQ ID NO:133 shown in Figure 77.

Figure 79 shows a nucleotide sequence (SEQ ID NO:135) of a native sequence PRO1275 (UNQ645) cDNA, wherein SEQ ID NO:135 is a clone designated herein as "DNA64888-1542". The start and stop codons are shown in bold and underlined font.

15 Figure 80 shows the amino acid sequence (SEQ ID NO:136) derived from the coding sequence of SEQ ID NO:135 shown in Figure 79.

Figure 81 shows a nucleotide sequence (SEQ ID NO:137) of a native sequence PRO1274 (UNQ644) cDNA, wherein SEQ ID NO:137 is a clone designated herein as "DNA64889-1542". The start and stop codons are shown in bold and underlined font.

20 Figure 82 shows the amino acid sequence (SEQ ID NO:138) derived from the coding sequence of SEQ ID NO:137 shown in Figure 81.

Figure 83 shows a nucleotide sequence (SEQ ID NO:139) of a native sequence PRO1412 (UNQ730) cDNA, wherein SEQ ID NO:139 is a clone designated herein as "DNA64897-1628". The start and stop codons are shown in bold and underlined font.

25 Figure 84 shows the amino acid sequence (SEQ ID NO:140) derived from the coding sequence of SEQ ID NO:139 shown in Figure 83.

Figure 85 shows a nucleotide sequence (SEQ ID NO:141) of a native sequence PRO1557 (UNQ765) cDNA, wherein SEQ ID NO:141 is a clone designated herein as "DNA64902-1667". The start and stop codons are shown in bold and underlined font.

30 Figure 86 shows the amino acid sequence (SEQ ID NO:142) derived from the coding sequence of SEQ ID NO:141 shown in Figure 85.

Figure 87 shows a nucleotide sequence (SEQ ID NO:143) of a native sequence PRO1286 (UNQ655) cDNA, wherein SEQ ID NO:143 is a clone designated herein as "DNA64903-1553". The start and stop codons are shown in bold and underlined font.

35 Figure 88 shows the amino acid sequence (SEQ ID NO:144) derived from the coding sequence of SEQ ID NO:143 shown in Figure 87.

Figure 89 shows a nucleotide sequence (SEQ ID NO:145) of a native sequence PRO1294 (UNQ663) cDNA, wherein SEQ ID NO:145 is a clone designated herein as "DNA64905-1558". The start and stop codons are shown in bold and underlined font.

Figure 90 shows the amino acid sequence (SEQ ID NO:146) derived from the coding sequence of SEQ ID NO:145 shown in Figure 89.

5 Figure 91 shows a nucleotide sequence (SEQ ID NO:147) of a native sequence PRO1347 (UNQ702) cDNA, wherein SEQ ID NO:147 is a clone designated herein as "DNA64950-1590". The start and stop codons are shown in bold and underlined font.

Figure 92 shows the amino acid sequence (SEQ ID NO:148) derived from the coding sequence of SEQ ID NO:147 shown in Figure 91.

10 Figure 93 shows a nucleotide sequence (SEQ ID NO:152) of a native sequence PRO1305 (UNQ671) cDNA, wherein SEQ ID NO:152 is a clone designated herein as "DNA64952-1568". The start and stop codons are shown in bold and underlined font.

Figure 94 shows the amino acid sequence (SEQ ID NO:153) derived from the coding sequence of SEQ ID NO:152 shown in Figure 93.

15 Figure 95 shows a nucleotide sequence (SEQ ID NO:157) of a native sequence PRO1273 (UNQ643) cDNA, wherein SEQ ID NO:157 is a clone designated herein as "DNA65402-1540". The start and stop codons are shown in bold and underlined font.

Figure 96 shows the amino acid sequence (SEQ ID NO:158) derived from the coding sequence of SEQ ID NO:157 shown in Figure 95.

20 Figure 97 shows a nucleotide sequence (SEQ ID NO:159) of a native sequence PRO1302 (UNQ668) cDNA, wherein SEQ ID NO:159 is a clone designated herein as "DNA65403-1565". The start and stop codons are shown in bold and underlined font.

Figure 98 shows the amino acid sequence (SEQ ID NO:160) derived from the coding sequence of SEQ ID NO:159 shown in Figure 97.

25 Figure 99 shows a nucleotide sequence (SEQ ID NO:161) of a native sequence PRO1283 (UNQ653) cDNA, wherein SEQ ID NO:161 is a clone designated herein as "DNA65404-1551". The start and stop codons are shown in bold and underlined font.

Figure 100 shows the amino acid sequence (SEQ ID NO:162) derived from the coding sequence of SEQ ID NO:161 shown in Figure 99.

30 Figure 101 shows a nucleotide sequence (SEQ ID NO:169) of a native sequence PRO1279 (UNQ649) cDNA, wherein SEQ ID NO:169 is a clone designated herein as "DNA65405-1547". The start and stop codons are shown in bold and underlined font.

Figure 102 shows the amino acid sequence (SEQ ID NO:170) derived from the coding sequence of SEQ ID NO:169 shown in Figure 101.

35 Figure 103 shows a nucleotide sequence (SEQ ID NO:179) of a native sequence PRO1304 (UNQ670) cDNA, wherein SEQ ID NO:179 is a clone designated herein as "DNA65406-1567". The start and stop codons are shown in bold and underlined font.

Figure 104 shows the amino acid sequence (SEQ ID NO:180) derived from the coding sequence of SEQ ID NO:179 shown in Figure 103.

Figure 105 shows a nucleotide sequence (SEQ ID NO:188) of a native sequence PRO1317 (UNQ683) cDNA, wherein SEQ ID NO:188 is a clone designated herein as "DNA65408-1578". The start and stop codons are shown in bold and underlined font.

5 Figure 106 shows the amino acid sequence (SEQ ID NO:189) derived from the coding sequence of SEQ ID NO:188 shown in Figure 105.

Figure 107 shows a nucleotide sequence (SEQ ID NO:193) of a native sequence PRO1303 (UNQ669) cDNA, wherein SEQ ID NO:193 is a clone designated herein as "DNA65409-1566". The start and stop codons are shown in bold and underlined font.

10 Figure 108 shows the amino acid sequence (SEQ ID NO:194) derived from the coding sequence of SEQ ID NO:193 shown in Figure 107.

Figure 109 shows a nucleotide sequence (SEQ ID NO:195) of a native sequence PRO1306 (UNQ672) cDNA, wherein SEQ ID NO:195 is a clone designated herein as "DNA65410-1569". The start and stop codons are shown in bold and underlined font.

15 Figure 110 shows the amino acid sequence (SEQ ID NO:196) derived from the coding sequence of SEQ ID NO:195 shown in Figure 109.

Figures 111A-B show a nucleotide sequence (SEQ ID NO:197) of a native sequence PRO1336 (UNQ691) cDNA, wherein SEQ ID NO:197 is a clone designated herein as "DNA65423-1595". The start and stop codons are shown in bold and underlined font.

20 Figure 112 shows the amino acid sequence (SEQ ID NO:198) derived from the coding sequence of SEQ ID NO:198 shown in Figures 111A-B.

Figure 113 shows a nucleotide sequence (SEQ ID NO:202) of a native sequence PRO1278 (UNQ648) cDNA, wherein SEQ ID NO:202 is a clone designated herein as "DNA66304-1546". The start and stop codons are shown in bold and underlined font.

25 Figure 114 shows the amino acid sequence (SEQ ID NO:203) derived from the coding sequence of SEQ ID NO:202 shown in Figure 113.

Figure 115 shows a nucleotide sequence (SEQ ID NO:209) of a native sequence PRO1298 (UNQ666) cDNA, wherein SEQ ID NO:209 is a clone designated herein as "DNA66511-1563". The start and stop codons are shown in bold and underlined font.

30 Figure 116 shows the amino acid sequence (SEQ ID NO:210) derived from the coding sequence of SEQ ID NO:209 shown in Figure 115.

Figure 117 shows a nucleotide sequence (SEQ ID NO:211) of a native sequence PRO1301 (UNQ667) cDNA, wherein SEQ ID NO:211 is a clone designated herein as "DNA66512-1564". The start and stop codons are shown in bold and underlined font.

35 Figure 118 shows the amino acid sequence (SEQ ID NO:212) derived from the coding sequence of SEQ ID NO:211 shown in Figure 117.

Figure 119 shows a nucleotide sequence (SEQ ID NO:213) of a native sequence PRO1268 (UNQ638) cDNA, wherein SEQ ID NO:213 is a clone designated herein as "DNA66519-1535". The start and stop codons are shown in bold and underlined font.

Figure 120 shows the amino acid sequence (SEQ ID NO:214) derived from the coding sequence of SEQ ID NO:213 shown in Figure 119.

5 Figure 121 shows a nucleotide sequence (SEQ ID NO:215) of a native sequence PRO1269 (UNQ639) cDNA, wherein SEQ ID NO:215 is a clone designated herein as "DNA66520-1536". The start and stop codons are shown in bold and underlined font.

Figure 122 shows the amino acid sequence (SEQ ID NO:216) derived from the coding sequence of SEQ ID NO:215 shown in Figure 121.

10 Figure 123 shows a nucleotide sequence (SEQ ID NO:217) of a native sequence PRO1327 (UNQ687) cDNA, wherein SEQ ID NO:217 is a clone designated herein as "DNA66521-1583". The start and stop codons are shown in bold and underlined font.

Figure 124 shows the amino acid sequence (SEQ ID NO:218) derived from the coding sequence of SEQ ID NO:217 shown in Figure 123.

15 Figure 125 shows a nucleotide sequence (SEQ ID NO:219) of a native sequence PRO1382 (UNQ718) cDNA, wherein SEQ ID NO:219 is a clone designated herein as "DNA66526-1616". The start and stop codons are shown in bold and underlined font.

Figure 126 shows the amino acid sequence (SEQ ID NO:220) derived from the coding sequence of SEQ ID NO:219 shown in Figure 125.

20 Figure 127 shows a nucleotide sequence (SEQ ID NO:224) of a native sequence PRO1328 (UNQ688) cDNA, wherein SEQ ID NO:224 is a clone designated herein as "DNA66658-1584". The start and stop codons are shown in bold and underlined font.

Figure 128 shows the amino acid sequence (SEQ ID NO:225) derived from the coding sequence of SEQ ID NO:224 shown in Figure 127.

25 Figure 129 shows a nucleotide sequence (SEQ ID NO:226) of a native sequence PRO1325 (UNQ685) cDNA, wherein SEQ ID NO:226 is a clone designated herein as "DNA66659-1593". The start and stop codons are shown in bold and underlined font.

Figure 130 shows the amino acid sequence (SEQ ID NO:227) derived from the coding sequence of SEQ ID NO:226 shown in Figure 129.

30 Figure 131 shows a nucleotide sequence (SEQ ID NO:228) of a native sequence PRO1340 (UNQ695) cDNA, wherein SEQ ID NO:228 is a clone designated herein as "DNA66663-1598". The start and stop codons are shown in bold and underlined font.

Figure 132 shows the amino acid sequence (SEQ ID NO:229) derived from the coding sequence of SEQ ID NO:228 shown in Figure 131.

35 Figure 133 shows a nucleotide sequence (SEQ ID NO:233) of a native sequence PRO1339 (UNQ694) cDNA, wherein SEQ ID NO:233 is a clone designated herein as "DNA66669-1597". The start and stop codons are shown in bold and underlined font.

Figure 134 shows the amino acid sequence (SEQ ID NO:234) derived from the coding sequence of SEQ ID NO:233 shown in Figure 133.

Figure 135 shows a nucleotide sequence (SEQ ID NO:235) of a native sequence PRO1337 (UNQ692) cDNA, wherein SEQ ID NO:235 is a clone designated herein as "DNA66672-1586". The start and stop codons are shown in bold and underlined font.

5 Figure 136 shows the amino acid sequence (SEQ ID NO:236) derived from the coding sequence of SEQ ID NO:235 shown in Figure 135.

Figure 137 shows a nucleotide sequence (SEQ ID NO:242) of a native sequence PRO1342 (UNQ697) cDNA, wherein SEQ ID NO:242 is a clone designated herein as "DNA66674-1599". The start and stop codons are shown in bold and underlined font.

10 Figure 138 shows the amino acid sequence (SEQ ID NO:243) derived from the coding sequence of SEQ ID NO:242 shown in Figure 137.

Figure 139 shows a nucleotide sequence (SEQ ID NO:247) of a native sequence PRO1343 (UNQ698) cDNA, wherein SEQ ID NO:247 is a clone designated herein as "DNA66675-1587". The start and stop codons are shown in bold and underlined font.

15 Figure 140 shows the amino acid sequence (SEQ ID NO:248) derived from the coding sequence of SEQ ID NO:247 shown in Figure 139.

Figure 141 shows a nucleotide sequence (SEQ ID NO:252) of a native sequence PRO1480 (UNQ749) cDNA, wherein SEQ ID NO:252 is a clone designated herein as "DNA67962-1649". The start and stop codons are shown in bold and underlined font.

20 Figure 142 shows the amino acid sequence (SEQ ID NO:253) derived from the coding sequence of SEQ ID NO:252 shown in Figure 141.

Figures 143A-B show a nucleotide sequence (SEQ ID NO:259) of a native sequence PRO1487 (UNQ756) cDNA, wherein SEQ ID NO:259 is a clone designated herein as "DNA68836-1656". The start and stop codons are shown in bold and underlined font.

25 Figure 144 shows the amino acid sequence (SEQ ID NO:260) derived from the coding sequence of SEQ ID NO:259 shown in Figures 143A-B.

Figure 145 shows a nucleotide sequence (SEQ ID NO:264) of a native sequence PRO1418 (UNQ732) cDNA, wherein SEQ ID NO:264 is a clone designated herein as "DNA68864-1629". The start and stop codons are shown in bold and underlined font.

30 Figure 146 shows the amino acid sequence (SEQ ID NO:265) derived from the coding sequence of SEQ ID NO:264 shown in Figure 145.

Figure 147 shows a nucleotide sequence (SEQ ID NO:266) of a native sequence PRO1472 (UNQ744) cDNA, wherein SEQ ID NO:266 is a clone designated herein as "DNA68866-1644". The start and stop codons are shown in bold and underlined font.

35 Figure 148 shows the amino acid sequence (SEQ ID NO:267) derived from the coding sequence of SEQ ID NO:266 shown in Figure 147.

Figure 149 shows a nucleotide sequence (SEQ ID NO:268) of a native sequence PRO1461 (UNQ742) cDNA, wherein SEQ ID NO:268 is a clone designated herein as "DNA68871-1638". The start and stop codons are shown in bold and underlined font.

Figure 150 shows the amino acid sequence (SEQ ID NO:269) derived from the coding sequence of SEQ ID NO:268 shown in Figure 149.

5 Figure 151 shows a nucleotide sequence (SEQ ID NO:270) of a native sequence PRO1410 (UNQ728) cDNA, wherein SEQ ID NO:270 is a clone designated herein as "DNA68874-1622". The start and stop codons are shown in bold and underlined font.

Figure 152 shows the amino acid sequence (SEQ ID NO:271) derived from the coding sequence of SEQ ID NO:270 shown in Figure 151.

10 Figure 153 shows a nucleotide sequence (SEQ ID NO:272) of a native sequence PRO1568 (UNQ774) cDNA, wherein SEQ ID NO:272 is a clone designated herein as "DNA68880-1676". The start and stop codons are shown in bold and underlined font.

Figure 154 shows the amino acid sequence (SEQ ID NO:273) derived from the coding sequence of SEQ ID NO:272 shown in Figure 153.

15 Figure 155 shows a nucleotide sequence (SEQ ID NO:274) of a native sequence PRO1570 (UNQ776) cDNA, wherein SEQ ID NO:274 is a clone designated herein as "DNA68885-1678". The start and stop codons are shown in bold and underlined font.

Figure 156 shows the amino acid sequence (SEQ ID NO:275) derived from the coding sequence of SEQ ID NO:274 shown in Figure 155.

20 Figure 157 shows a nucleotide sequence (SEQ ID NO:276) of a native sequence PRO1317 (UNQ783) cDNA, wherein SEQ ID NO:276 is a clone designated herein as "DNA71166-1685". The start and stop codons are shown in bold and underlined font.

Figure 158 shows the amino acid sequence (SEQ ID NO:277) derived from the coding sequence of SEQ ID NO:276 shown in Figure 157.

25 Figure 159 shows a nucleotide sequence (SEQ ID NO:281) of a native sequence PRO1780 (UNQ842) cDNA, wherein SEQ ID NO:281 is a clone designated herein as "DNA71169-1709". The start and stop codons are shown in bold and underlined font.

Figure 160 shows the amino acid sequence (SEQ ID NO:282) derived from the coding sequence of SEQ ID NO:281 shown in Figure 159.

30 Figure 161 shows a nucleotide sequence (SEQ ID NO:286) of a native sequence PRO1486 (UNQ755) cDNA, wherein SEQ ID NO:286 is a clone designated herein as "DNA71180-1655". The start and stop codons are shown in bold and underlined font.

Figure 162 shows the amino acid sequence (SEQ ID NO:287) derived from the coding sequence of SEQ ID NO:286 shown in Figure 161.

35 Figure 163 shows a nucleotide sequence (SEQ ID NO:291) of a native sequence PRO1433 (UNQ738) cDNA, wherein SEQ ID NO:291 is a clone designated herein as "DNA71184-1634". The start and stop codons are shown in bold and underlined font.

Figure 164 shows the amino acid sequence (SEQ ID NO:292) derived from the coding sequence of SEQ ID NO:291 shown in Figure 163.

Figure 165 shows a nucleotide sequence (SEQ ID NO:296) of a native sequence PRO1490 (UNQ759) cDNA, wherein SEQ ID NO:296 is a clone designated herein as "DNA71213-1659". The start and stop codons are shown in bold and underlined font.

5 Figure 166 shows the amino acid sequence (SEQ ID NO:297) derived from the coding sequence of SEQ ID NO:296 shown in Figure 165.

Figure 167 shows a nucleotide sequence (SEQ ID NO:301) of a native sequence PRO1482 (UNQ751) cDNA, wherein SEQ ID NO:301 is a clone designated herein as "DNA71234-1651". The start and stop codons are shown in bold and underlined font.

10 Figure 168 shows the amino acid sequence (SEQ ID NO:302) derived from the coding sequence of SEQ ID NO:301 shown in Figure 167.

Figure 169 shows a nucleotide sequence (SEQ ID NO:303) of a native sequence PRO1446 (UNQ740) cDNA, wherein SEQ ID NO:303 is a clone designated herein as "DNA71277-1636". The start and stop codons are shown in bold and underlined font.

15 Figure 170 shows the amino acid sequence (SEQ ID NO:304) derived from the coding sequence of SEQ ID NO:303 shown in Figure 169.

Figure 171 shows a nucleotide sequence (SEQ ID NO:305) of a native sequence PRO1558 (UNQ766) cDNA, wherein SEQ ID NO:305 is a clone designated herein as "DNA71282-1668". The start and stop codons are shown in bold and underlined font.

20 Figure 172 shows the amino acid sequence (SEQ ID NO:306) derived from the coding sequence of SEQ ID NO:305 shown in Figure 171.

Figure 173 shows a nucleotide sequence (SEQ ID NO:307) of a native sequence PRO1604 (UNQ785) cDNA, wherein SEQ ID NO:307 is a clone designated herein as "DNA71286-1687". The start and stop codons are shown in bold and underlined font.

25 Figure 174 shows the amino acid sequence (SEQ ID NO:308) derived from the coding sequence of SEQ ID NO:307 shown in Figure 173.

Figure 175 shows a nucleotide sequence (SEQ ID NO:309) of a native sequence PRO1491 (UNQ760) cDNA, wherein SEQ ID NO:309 is a clone designated herein as "DNA71883-1660". The start and stop codons are shown in bold and underlined font.

30 Figure 176 shows the amino acid sequence (SEQ ID NO:310) derived from the coding sequence of SEQ ID NO:309 shown in Figure 175.

Figure 177 shows a nucleotide sequence (SEQ ID NO:314) of a native sequence PRO1431 (UNQ737) cDNA, wherein SEQ ID NO:314 is a clone designated herein as "DNA73401-1633". The start and stop codons are shown in bold and underlined font.

35 Figure 178 shows the amino acid sequence (SEQ ID NO:315) derived from the coding sequence of SEQ ID NO:314 shown in Figure 177.

Figures 179A-B show a nucleotide sequence (SEQ ID NO:316) of a native sequence PRO1563 (UNQ769) cDNA, wherein SEQ ID NO:316 is a clone designated herein as "DNA73492-1671". The start and stop codons are shown in bold and underlined font.

Figure 180 shows the amino acid sequence (SEQ ID NO:317) derived from the coding sequence of SEQ ID NO:316 shown in Figures 179A-B.

5 Figure 181 shows a nucleotide sequence (SEQ ID NO:321) of a native sequence PRO1565 (UNQ771) cDNA, wherein SEQ ID NO:321 is a clone designated herein as "DNA73727-1673". The start and stop codons are shown in bold and underlined font.

Figure 182 shows the amino acid sequence (SEQ ID NO:322) derived from the coding sequence of SEQ ID NO:321 shown in Figure 181.

10 Figure 183 shows a nucleotide sequence (SEQ ID NO:323) of a native sequence PRO1571 (UNQ777) cDNA, wherein SEQ ID NO:323 is a clone designated herein as "DNA73730-1679". The start and stop codons are shown in bold and underlined font.

Figure 184 shows the amino acid sequence (SEQ ID NO:324) derived from the coding sequence of SEQ ID NO:323 shown in Figure 183.

15 Figure 185 shows a nucleotide sequence (SEQ ID NO:325) of a native sequence PRO1572 (UNQ778) cDNA, wherein SEQ ID NO:325 is a clone designated herein as "DNA73734-1680". The start and stop codons are shown in bold and underlined font.

Figure 186 shows the amino acid sequence (SEQ ID NO:326) derived from the coding sequence of SEQ ID NO:325 shown in Figure 185.

20 Figure 187 shows a nucleotide sequence (SEQ ID NO:327) of a native sequence PRO1573 (UNQ779) cDNA, wherein SEQ ID NO:327 is a clone designated herein as "DNA73735-1681". The start and stop codons are shown in bold and underlined font.

Figure 188 shows the amino acid sequence (SEQ ID NO:328) derived from the coding sequence of SEQ ID NO:327 shown in Figure 187.

25 Figure 189 shows a nucleotide sequence (SEQ ID NO:329) of a native sequence PRO1488 (UNQ757) cDNA, wherein SEQ ID NO:329 is a clone designated herein as "DNA73736-1657". The start and stop codons are shown in bold and underlined font.

Figure 190 shows the amino acid sequence (SEQ ID NO:330) derived from the coding sequence of SEQ ID NO:329 shown in Figure 189.

30 Figure 191 shows a nucleotide sequence (SEQ ID NO:331) of a native sequence PRO1489 (UNQ758) cDNA, wherein SEQ ID NO:331 is a clone designated herein as "DNA73737-1658". The start and stop codons are shown in bold and underlined font.

Figure 192 shows the amino acid sequence (SEQ ID NO:332) derived from the coding sequence of SEQ ID NO:331 shown in Figure 191.

35 Figure 193 shows a nucleotide sequence (SEQ ID NO:333) of a native sequence PRO1474 (UNQ745) cDNA, wherein SEQ ID NO:333 is a clone designated herein as "DNA73739-1645". The start and stop codons are shown in bold and underlined font.

Figure 194 shows the amino acid sequence (SEQ ID NO:334) derived from the coding sequence of SEQ ID NO:333 shown in Figure 193.

Figure 195 shows a nucleotide sequence (SEQ ID NO:335) of a native sequence PRO1508 (UNQ761) cDNA, wherein SEQ ID NO:335 is a clone designated herein as "DNA73742-1662". The start and stop codons are shown in bold and underlined font.

5 Figure 196 shows the amino acid sequence (SEQ ID NO:336) derived from the coding sequence of SEQ ID NO:335 shown in Figure 195.

Figure 197 shows a nucleotide sequence (SEQ ID NO:337) of a native sequence PRO1555 (UNQ763) cDNA, wherein SEQ ID NO:337 is a clone designated herein as "DNA73744-1665". The start and stop codons are shown in bold and underlined font.

10 Figure 198 shows the amino acid sequence (SEQ ID NO:338) derived from the coding sequence of SEQ ID NO:337 shown in Figure 197.

Figure 199 shows a nucleotide sequence (SEQ ID NO:339) of a native sequence PRO1485 (UNQ754) cDNA, wherein SEQ ID NO:339 is a clone designated herein as "DNA73746-1654". The start and stop codons are shown in bold and underlined font.

15 Figure 200 shows the amino acid sequence (SEQ ID NO:340) derived from the coding sequence of SEQ ID NO:339 shown in Figure 199.

Figure 201 shows a nucleotide sequence (SEQ ID NO:346) of a native sequence PRO1564 (UNQ770) cDNA, wherein SEQ ID NO:346 is a clone designated herein as "DNA73760-1672". The start and stop codons are shown in bold and underlined font.

20 Figure 202 shows the amino acid sequence (SEQ ID NO:347) derived from the coding sequence of SEQ ID NO:346 shown in Figure 201.

Figure 203 shows a nucleotide sequence (SEQ ID NO:351) of a native sequence PRO1755 (UNQ828) cDNA, wherein SEQ ID NO:351 is a clone designated herein as "DNA76396-1698". The start and stop codons are shown in bold and underlined font.

25 Figure 204 shows the amino acid sequence (SEQ ID NO:352) derived from the coding sequence of SEQ ID NO:351 shown in Figure 203.

Figure 205 shows a nucleotide sequence (SEQ ID NO:353) of a native sequence PRO1757 (UNQ830) cDNA, wherein SEQ ID NO:353 is a clone designated herein as "DNA76398-1699". The start and stop codons are shown in bold and underlined font.

30 Figure 206 shows the amino acid sequence (SEQ ID NO:354) derived from the coding sequence of SEQ ID NO:353 shown in Figure 205.

Figure 207 shows a nucleotide sequence (SEQ ID NO:355) of a native sequence PRO1758 (UNQ831) cDNA, wherein SEQ ID NO:355 is a clone designated herein as "DNA76399-1700". The start and stop codons are shown in bold and underlined font.

35 Figure 208 shows the amino acid sequence (SEQ ID NO:356) derived from the coding sequence of SEQ ID NO:355 shown in Figure 207.

Figure 209 shows a nucleotide sequence (SEQ ID NO:357) of a native sequence PRO1575 (UNQ781) cDNA, wherein SEQ ID NO:357 is a clone designated herein as "DNA76401-1683". The start and stop codons are shown in bold and underlined font.

Figure 210 shows the amino acid sequence (SEQ ID NO:358) derived from the coding sequence of SEQ ID NO:357 shown in Figure 209.

5 Figure 211 shows a nucleotide sequence (SEQ ID NO:363) of a native sequence PRO1787 (UNQ849) cDNA, wherein SEQ ID NO:363 is a clone designated herein as "DNA76510-2504". The start and stop codons are shown in bold and underlined font.

Figure 212 shows the amino acid sequence (SEQ ID NO:364) derived from the coding sequence of SEQ ID NO:363 shown in Figure 211.

10 Figure 213 shows a nucleotide sequence (SEQ ID NO:365) of a native sequence PRO1781 (UNQ843) cDNA, wherein SEQ ID NO:365 is a clone designated herein as "DNA76522-2500". The start and stop codons are shown in bold and underlined font.

Figure 214 shows the amino acid sequence (SEQ ID NO:366) derived from the coding sequence of SEQ ID NO:365 shown in Figure 213.

15 Figure 215 shows a nucleotide sequence (SEQ ID NO:371) of a native sequence PRO1556 (UNQ764) cDNA, wherein SEQ ID NO:371 is a clone designated herein as "DNA76529-1666". The start and stop codons are shown in bold and underlined font.

Figure 216 shows the amino acid sequence (SEQ ID NO:372) derived from the coding sequence of SEQ ID NO:371 shown in Figure 215.

20 Figure 217 shows a nucleotide sequence (SEQ ID NO:373) of a native sequence PRO1759 (UNQ832) cDNA, wherein SEQ ID NO:373 is a clone designated herein as "DNA76531-1701". The start and stop codons are shown in bold and underlined font.

Figure 218 shows the amino acid sequence (SEQ ID NO:374) derived from the coding sequence of SEQ ID NO:373 shown in Figure 217.

25 Figure 219 shows a nucleotide sequence (SEQ ID NO:375) of a native sequence PRO1760 (UNQ833) cDNA, wherein SEQ ID NO:375 is a clone designated herein as "DNA76532-1702". The start and stop codons are shown in bold and underlined font.

Figure 220 shows the amino acid sequence (SEQ ID NO:376) derived from the coding sequence of SEQ ID NO:375 shown in Figure 219.

30 Figure 221 shows a nucleotide sequence (SEQ ID NO:377) of a native sequence PRO1561 (UNQ768) cDNA, wherein SEQ ID NO:377 is a clone designated herein as "DNA76538-1670". The start and stop codons are shown in bold and underlined font.

Figure 222 shows the amino acid sequence (SEQ ID NO:378) derived from the coding sequence of SEQ ID NO:377 shown in Figure 221.

35 Figure 223 shows a nucleotide sequence (SEQ ID NO:382) of a native sequence PRO1567 (UNQ773) cDNA, wherein SEQ ID NO:382 is a clone designated herein as "DNA76541-1675". The start and stop codons are shown in bold and underlined font.

Figure 224 shows the amino acid sequence (SEQ ID NO:383) derived from the coding sequence of SEQ ID NO:382 shown in Figure 223.

Figure 225 shows a nucleotide sequence (SEQ ID NO:384) of a native sequence PRO1693 (UNQ803) cDNA, wherein SEQ ID NO:384 is a clone designated herein as "DNA77301-1693". The start and stop codons are shown in bold and underlined font.

5 Figure 226 shows the amino acid sequence (SEQ ID NO:385) derived from the coding sequence of SEQ ID NO:384 shown in Figure 225.

Figure 227 shows a nucleotide sequence (SEQ ID NO:389) of a native sequence PRO1784 (UNQ846) cDNA, wherein SEQ ID NO:389 is a clone designated herein as "DNA77303-2502". The start and stop codons are shown in bold and underlined font.

10 Figure 228 shows the amino acid sequence (SEQ ID NO:390) derived from the coding sequence of SEQ ID NO:389 shown in Figure 227.

Figure 229 shows a nucleotide sequence (SEQ ID NO:394) of a native sequence PRO1605 (UNQ786) cDNA, wherein SEQ ID NO:394 is a clone designated herein as "DNA77648-1688". The start and stop codons are shown in bold and underlined font.

15 Figure 230 shows the amino acid sequence (SEQ ID NO:395) derived from the coding sequence of SEQ ID NO:394 shown in Figure 229.

Figure 231 shows a nucleotide sequence (SEQ ID NO:396) of a native sequence PRO1788 (UNQ850) cDNA, wherein SEQ ID NO:396 is a clone designated herein as "DNA77652-2505". The start and stop codons are shown in bold and underlined font.

20 Figure 232 shows the amino acid sequence (SEQ ID NO:397) derived from the coding sequence of SEQ ID NO:396 shown in Figure 231.

Figure 233 shows a nucleotide sequence (SEQ ID NO:401) of a native sequence PRO1801 (UNQ852) cDNA, wherein SEQ ID NO:401 is a clone designated herein as "DNA83500-2506". The start and stop codons are shown in bold and underlined font.

25 Figure 234 shows the amino acid sequence (SEQ ID NO:402) derived from the coding sequence of SEQ ID NO:401 shown in Figure 233.

Figure 235 shows a nucleotide sequence (SEQ ID NO:405) of a native sequence UCP4 cDNA, wherein SEQ ID NO:405 is a clone designated herein as "DNA77568-1626". The start and stop codons are shown in bold and underlined font.

30 Figure 236 shows the amino acid sequence (SEQ ID NO:406) derived from the coding sequence of SEQ ID NO:405 shown in Figure 235.

Figure 237 shows a nucleotide sequence (SEQ ID NO:409) of a native sequence PRO193 cDNA, wherein SEQ ID NO:409 is a clone designated herein as "DNA23322-1393". The start and stop codons are shown in bold and underlined font.

35 Figure 238 shows the amino acid sequence (SEQ ID NO:410) derived from the coding sequence of SEQ ID NO:409 shown in Figure 237.

Figure 239 shows a nucleotide sequence (SEQ ID NO:414) of a native sequence PRO1130 cDNA, wherein SEQ ID NO:414 is a clone designated herein as "DNA59814-1486". The start and stop codons are shown in bold and underlined font.

Figure 240 shows the amino acid sequence (SEQ ID NO:415) derived from the coding sequence of SEQ ID NO:414 shown in Figure 239.

5 Figure 241 shows a nucleotide sequence (SEQ ID NO:422) of a native sequence PRO1335 cDNA, wherein SEQ ID NO:422 is a clone designated herein as "DNA62812-1594". The start and stop codons are shown in bold and underlined font.

Figure 242 shows the amino acid sequence (SEQ ID NO:423) derived from the coding sequence of SEQ ID NO:422 shown in Figure 241.

10 Figure 243 shows a nucleotide sequence (SEQ ID NO:428) of a native sequence PRO1329 cDNA, wherein SEQ ID NO:428 is a clone designated herein as "DNA66660-1585". The start and stop codons are shown in bold and underlined font.

Figure 244 shows the amino acid sequence (SEQ ID NO:429) derived from the coding sequence of SEQ ID NO:428 shown in Figure 243.

15 Figure 245 shows a nucleotide sequence (SEQ ID NO:430) of a native sequence PRO1550 cDNA, wherein SEQ ID NO:430 is a clone designated herein as "DNA76393-1664". The start and stop codons are shown in bold and underlined font.

Figure 246 shows the amino acid sequence (SEQ ID NO:431) derived from the coding sequence of SEQ ID NO:430 shown in Figure 245.

20 Figures 247A-D show hypothetical exemplifications for using the below described method to determine % amino acid sequence identity (Figures 247A-B) and % nucleic acid sequence identity (Figures 247C-D) using the ALIGN-2 sequence comparison computer program, wherein "PRO" represents the amino acid sequence of a hypothetical PEACH polypeptide of interest, "Comparison Protein" represents the amino acid sequence of a polypeptide against which the "PRO" polypeptide of interest is being compared, "PRO-DNA" represents a
25 hypothetical PEACH-encoding nucleic acid sequence of interest, "Comparison DNA" represents the nucleotide sequence of a nucleic acid molecule against which the "PRO-DNA" nucleic acid molecule of interest is being compared, "X", "Y" and "Z" each represent different hypothetical amino acid residues and "N", "L" and "V" each represent different hypothetical nucleotides.

30 Figures 248A-Q provide the complete source code for the ALIGN-2 sequence comparison computer program. This source code may be routinely compiled for use on a UNIX operating system to provide the ALIGN-2 sequence comparison computer program.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

I. Definitions

35 The terms "PRO polypeptide" and "PRO" or "UCP" as used herein and when immediately followed by a numerical designation refer to various polypeptides, wherein the complete designation (i.e., PRO/number) refers to specific polypeptide sequences as described herein. The terms "PRO/number polypeptide" and

"PRO/number" wherein the term "number" is provided as an actual numerical designation as used herein encompass native sequence polypeptides and polypeptide variants (which are further defined herein). The PRO polypeptides described herein may be isolated from a variety of sources, such as from human tissue types or from another source, or prepared by recombinant or synthetic methods.

5 A "native sequence PRO polypeptide" or "UCP" comprises a polypeptide having the same amino acid sequence as the corresponding PRO polypeptide derived from nature. Such native sequence PRO polypeptides can be isolated from nature or can be produced by recombinant or synthetic means. The term "native sequence PRO polypeptide" specifically encompasses naturally-occurring truncated or secreted forms of the specific PRO polypeptide (*e.g.*, an extracellular domain sequence), naturally-occurring variant forms (*e.g.*, alternatively spliced forms) and naturally-occurring allelic variants of the polypeptide. In various embodiments of the
10 invention, native sequence PRO polypeptides are mature or full-length native sequence polypeptides comprising the full-length amino acids sequences shown in the accompanying figures. Start and stop codons are shown in bold font and underlined in the figures. However, while the PRO polypeptide disclosed in the accompanying figures are shown to begin with methionine residues designated herein as amino acid position 1 in the figures, it is conceivable and possible that other methionine residues located either upstream or downstream from the
15 amino acid position 1 in the figures may be employed as the starting amino acid residue for the PRO polypeptides.

The PRO polypeptide "extracellular domain" or "ECD" refers to a form of the PRO polypeptide which is essentially free of the transmembrane and cytoplasmic domains. Ordinarily, a PRO polypeptide ECD will have less than 1% of such transmembrane and/or cytoplasmic domains and preferably, will have less than 0.5% of
20 such domains. It will be understood that any transmembrane domains identified for the PRO polypeptides of the present invention are identified pursuant to criteria routinely employed in the art for identifying that type of hydrophobic domain. The exact boundaries of a transmembrane domain may vary but most likely by no more than about 5 amino acids at either end of the domain as initially identified herein. Optionally, therefore, an extracellular domain of a PRO polypeptide may contain from about 5 or fewer amino acids on either side of the
25 transmembrane domain/extracellular domain boundary as identified in the Examples or specification and such polypeptides, with or without the associated signal peptide, and nucleic acid encoding them, are contemplated by the present invention.

The approximate location of the "signal peptides" of the various PRO polypeptides disclosed herein are shown in the accompanying figures. It is noted, however, that the C-terminal boundary of a signal peptide may
30 vary, but most likely by no more than about 5 amino acids on either side of the signal peptide C-terminal boundary as initially identified herein, wherein the C-terminal boundary of the signal peptide may be identified pursuant to criteria routinely employed in the art for identifying that type of amino acid sequence element (*e.g.*, Nielsen et al., Prot. Eng. 10:1-6 (1997) and von Heinje et al., Nucl. Acids. Res. 14:4683-4690 (1986)). Moreover, it is also recognized that, in some cases, cleavage of a signal sequence from a secreted polypeptide
35 is not entirely uniform, resulting in more than one secreted species. These mature polypeptides, where the signal peptide is cleaved within no more than about 5 amino acids on either side of the C-terminal boundary of the signal peptide as identified herein, and the polynucleotides encoding them, are contemplated by the present

invention.

"PRO polypeptide variant" means an active PRO polypeptide as defined above or below having at least about 80% amino acid sequence identity with a full-length native sequence PRO polypeptide sequence as disclosed herein, a PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Such PRO polypeptide variants include, for instance, PRO polypeptides wherein one or more amino acid residues are added, or deleted, at the N- or C-terminus of the full-length native amino acid sequence. Ordinarily, a PRO polypeptide variant will have at least about 80% amino acid sequence identity, preferably at least about 81% amino acid sequence identity, more preferably at least about 82% amino acid sequence identity, more preferably at least about 83% amino acid sequence identity, more preferably at least about 84% amino acid sequence identity, more preferably at least about 85% amino acid sequence identity, more preferably at least about 86% amino acid sequence identity, more preferably at least about 87% amino acid sequence identity, more preferably at least about 88% amino acid sequence identity, more preferably at least about 89% amino acid sequence identity, more preferably at least about 90% amino acid sequence identity, more preferably at least about 91% amino acid sequence identity, more preferably at least about 92% amino acid sequence identity, more preferably at least about 93% amino acid sequence identity, more preferably at least about 94% amino acid sequence identity, more preferably at least about 95% amino acid sequence identity, more preferably at least about 96% amino acid sequence identity, more preferably at least about 97% amino acid sequence identity, more preferably at least about 98% amino acid sequence identity and most preferably at least about 99% amino acid sequence identity with a full-length native sequence PRO polypeptide sequence as disclosed herein, a PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Ordinarily, PRO variant polypeptides are at least about 10 amino acids in length, often at least about 20 amino acids in length, more often at least about 30 amino acids in length, more often at least about 40 amino acids in length, more often at least about 50 amino acids in length, more often at least about 60 amino acids in length, more often at least about 70 amino acids in length, more often at least about 80 amino acids in length, more often at least about 90 amino acids in length, more often at least about 100 amino acids in length, more often at least about 150 amino acids in length, more often at least about 200 amino acids in length, more often at least about 300 amino acids in length, or more.

"Percent (%) amino acid sequence identity" with respect to the PRO polypeptide sequences identified herein is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific PRO polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed

to achieve maximal alignment over the full length of the sequences being compared. For purposes herein, however, % amino acid sequence identity values are generated using the WU-BLAST-2 computer program (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Most of the WU-BLAST-2 search parameters are set to the default values. Those not set to default values, i.e., the adjustable parameters, are set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold (T) = 11, and scoring matrix = BLOSUM62. For purposes herein, a % amino acid sequence identity value is determined by dividing (a) the number of matching identical amino acid residues between the amino acid sequence of the PRO polypeptide of interest having a sequence derived from the native PRO polypeptide and the comparison amino acid sequence of interest (i.e., the sequence against which the PRO polypeptide of interest is being compared which may be a PRO variant polypeptide) as determined by WU-BLAST-2 by (b) the total number of amino acid residues of the PRO polypeptide of interest. For example, in the statement "a polypeptide comprising an the amino acid sequence A which has or having at least 80% amino acid sequence identity to the amino acid sequence B", the amino acid sequence A is the comparison amino acid sequence of interest and the amino acid sequence B is the amino acid sequence of the PRO polypeptide of interest.

Unless specifically stated otherwise, all % amino acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the WU-BLAST-2 computer program. However, % amino acid sequence identity values may also be obtained as described below by using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Figures 248A-Q. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc. and the source code shown in Figures 248A-Q has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., South San Francisco, California or may be compiled from the source code provided in Figures 248A-Q. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

100 times the fraction X/Y

where X is the number of amino acid residues scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A. As examples of % amino acid sequence identity calculations using this method, Figures 247A-B demonstrate how to calculate the % amino acid sequence identity of the amino acid sequence designated

"Comparison Protein" to the amino acid sequence designated "PRO".

Percent amino acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., *Nucleic Acids Res.* 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from <http://www.ncbi.nlm.nih.gov>. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example,

5 unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

In situations where NCBI-BLAST2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B

10 (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

$$100 \text{ times the fraction } X/Y$$

15 where X is the number of amino acid residues scored as identical matches by the sequence alignment program NCBI-BLAST2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A.

20 "PRO variant polynucleotide" or "PRO variant nucleic acid sequence" means a nucleic acid molecule which encodes an active PRO polypeptide as defined below and which has at least about 80% nucleic acid sequence identity with a nucleotide acid sequence encoding a full-length native sequence PRO polypeptide sequence as disclosed herein, a full-length native sequence PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein.

Ordinarily, a PRO variant polynucleotide will have at least about 80% nucleic acid sequence identity, more preferably at least about 81% nucleic acid sequence identity, more preferably at least about 82% nucleic acid sequence identity, more preferably at least about 83% nucleic acid sequence identity, more preferably at least about 84% nucleic acid sequence identity, more preferably at least about 85% nucleic acid sequence identity,

25 more preferably at least about 86% nucleic acid sequence identity, more preferably at least about 87% nucleic acid sequence identity, more preferably at least about 88% nucleic acid sequence identity, more preferably at least about 89% nucleic acid sequence identity, more preferably at least about 90% nucleic acid sequence identity, more preferably at least about 91% nucleic acid sequence identity, more preferably at least about 92% nucleic acid sequence identity, more preferably at least about 93% nucleic acid sequence identity, more preferably at least about 94% nucleic acid sequence identity, more preferably at least about 95% nucleic acid sequence identity, more preferably at least about 96% nucleic acid sequence identity, more preferably at least about 97% nucleic acid sequence identity, more preferably at least about 98% nucleic acid sequence identity and

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yet more preferably at least about 99% nucleic acid sequence identity with the nucleic acid sequence encoding a full-length native sequence PRO polypeptide sequence as disclosed herein, a full-length native sequence PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal sequence, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Variants do not encompass the native nucleotide sequence.

5 Ordinarily, PRO variant polynucleotides are at least about 30 nucleotides in length, often at least about 60 nucleotides in length, more often at least about 90 nucleotides in length, more often at least about 120 nucleotides in length, more often at least about 150 nucleotides in length, more often at least about 180 nucleotides in length, more often at least about 210 nucleotides in length, more often at least about 240 nucleotides in length, more often at least about 270 nucleotides in length, more often at least about 300
10 nucleotides in length, more often at least about 450 nucleotides in length, more often at least about 600 nucleotides in length, more often at least about 900 nucleotides in length, or more.

"Percent (%) nucleic acid sequence identity" with respect to PRO-encoding nucleic acid sequences identified herein is defined as the percentage of nucleotides in a candidate sequence that are identical with the nucleotides in the PRO nucleic acid sequence of interest, after aligning the sequences and introducing gaps, if
15 necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent nucleic acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. For purposes herein, however, % nucleic acid sequence identity values are generated using the WU-BLAST-2 computer program (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Most of the WU-
20 BLAST-2 search parameters are set to the default values. Those not set to default values, i.e., the adjustable parameters, are set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold (T) = 11, and scoring matrix = BLOSUM62. For purposes herein, a % nucleic acid sequence identity value is determined by dividing (a) the number of matching identical nucleotides between the nucleic acid sequence of the PRO polypeptide-encoding nucleic acid molecule of interest having a sequence derived from the native
25 sequence PRO polypeptide-encoding nucleic acid and the comparison nucleic acid molecule of interest (i.e., the sequence against which the PRO polypeptide-encoding nucleic acid molecule of interest is being compared which may be a variant PRO polynucleotide) as determined by WU-BLAST-2 by (b) the total number of nucleotides of the PRO polypeptide-encoding nucleic acid molecule of interest. For example, in the statement "an isolated nucleic acid molecule comprising a nucleic acid sequence A which has or having at least 80% nucleic acid
30 sequence identity to the nucleic acid sequence B", the nucleic acid sequence A is the comparison nucleic acid molecule of interest and the nucleic acid sequence B is the nucleic acid sequence of the PRO polypeptide-encoding nucleic acid molecule of interest.

Unless specifically stated otherwise, all % nucleic acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the WU-BLAST-2 computer program. However,
35 % nucleic acid sequence identity values may also be obtained as described below by using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Figures 248A-Q. The ALIGN-2 sequence comparison computer program was authored by

Genentech, Inc. and the source code shown in Figures 248A-Q has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available through Genentech, Inc., South San Francisco, California or may be compiled from the source code provided in Figures 248A-Q. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence
5 comparison parameters are set by the ALIGN-2 program and do not vary.

In situations where ALIGN-2 is employed for nucleic acid sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

10

$$100 \text{ times the fraction } W/Z$$

where W is the number of nucleotides scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will be
15 appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to C. As examples of % nucleic acid sequence identity calculations, Figures 247C-D demonstrate how to calculate the % nucleic acid sequence identity of the nucleic acid sequence designated "Comparison DNA" to the nucleic acid sequence designated "PRO-DNA".

20 Percent nucleic acid sequence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res. 25:3389-3402 (1997)). The NCBI-BLAST2 sequence comparison program may be downloaded from <http://www.ncbi.nlm.nih.gov>. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass
25 e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

In situations where NCBI-BLAST2 is employed for sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid
30 sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

$$100 \text{ times the fraction } W/Z$$

where W is the number of nucleotides scored as identical matches by the sequence alignment program NCBI-BLAST2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will
35 be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to

C.

In other embodiments, PRO variant polynucleotides are nucleic acid molecules that encode an active PRO polypeptide and which are capable of hybridizing, preferably under stringent hybridization and wash conditions, to nucleotide sequences encoding a full-length PRO polypeptide as disclosed herein. PRO variant polypeptides may be those that are encoded by a PRO variant polynucleotide.

- 5 The term "positives", in the context of sequence comparison performed as described above, includes residues in the sequences compared that are not identical but have similar properties (e.g. as a result of conservative substitutions, see Table 1 below). For purposes herein, the % value of positives is determined by dividing (a) the number of amino acid residues scoring a positive value between the PRO polypeptide amino acid sequence of interest having a sequence derived from the native PRO polypeptide sequence and the comparison
10 amino acid sequence of interest (i.e., the amino acid sequence against which the PRO polypeptide sequence is being compared) as determined in the BLOSUM62 matrix of WU-BLAST-2 by (b) the total number of amino acid residues of the PRO polypeptide of interest.

- Unless specifically stated otherwise, the % value of positives is calculated as described in the immediately preceding paragraph. However, in the context of the amino acid sequence identity comparisons
15 performed as described for ALIGN-2 and NCBI-BLAST2 above, includes amino acid residues in the sequences compared that are not only identical, but also those that have similar properties. Amino acid residues that score a positive value to an amino acid residue of interest are those that are either identical to the amino acid residue of interest or are a preferred substitution (as defined in Table 1 below) of the amino acid residue of interest.

- For amino acid sequence comparisons using ALIGN-2 or NCBI-BLAST2, the % value of positives of
20 a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % positives to, with, or against a given amino acid sequence B) is calculated as follows:

$$100 \text{ times the fraction } X/Y$$

- 25 where X is the number of amino acid residues scoring a positive value as defined above by the sequence alignment program ALIGN-2 or NCBI-BLAST2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % positives of A to B will not equal the % positives
30 of B to A.

- "Isolated," when used to describe the various polypeptides disclosed herein, means polypeptide that has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials that would typically interfere with diagnostic or therapeutic uses for the polypeptide, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous
35 solutes. In preferred embodiments, the polypeptide will be purified (1) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (2) to homogeneity by SDS-PAGE under non-reducing or reducing conditions using Coomassie blue or, preferably,

silver stain. Isolated polypeptide includes polypeptide *in situ* within recombinant cells, since at least one component of the PRO polypeptide natural environment will not be present. Ordinarily, however, isolated polypeptide will be prepared by at least one purification step.

5 An "isolated" PRO polypeptide-encoding nucleic acid is a nucleic acid molecule that is identified and separated from at least one contaminant nucleic acid molecule with which it is ordinarily associated in the natural source of the PRO polypeptide nucleic acid. An isolated PRO polypeptide nucleic acid molecule is other than
10 in the form or setting in which it is found in nature. Isolated PRO polypeptide nucleic acid molecules therefore are distinguished from the specific PRO polypeptide nucleic acid molecule as it exists in natural cells. However, an isolated PRO polypeptide nucleic acid molecule includes PRO polypeptide nucleic acid molecules contained in cells that ordinarily express the PRO polypeptide where, for example, the nucleic acid molecule is in a chromosomal location different from that of natural cells.

The term "control sequences" refers to DNA sequences necessary for the expression of an operably linked coding sequence in a particular host organism. The control sequences that are suitable for prokaryotes, for example, include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

15 Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally,
20 "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice.

The term "antibody" is used in the broadest sense and specifically covers, for example, single anti-PRO
25 monoclonal antibodies (including agonist, antagonist, and neutralizing antibodies), anti-PRO antibody compositions with polyepitopic specificity, single chain anti-PRO antibodies, and fragments of anti-PRO antibodies (see below). The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally-occurring mutations that may be present in minor amounts.

30 "Stringency" of hybridization reactions is readily determinable by one of ordinary skill in the art, and generally is an empirical calculation dependent upon probe length, washing temperature, and salt concentration. In general, longer probes require higher temperatures for proper annealing, while shorter probes need lower temperatures. Hybridization generally depends on the ability of denatured DNA to reanneal when complementary strands are present in an environment below their melting temperature. The higher the degree
35 of desired homology between the probe and hybridizable sequence, the higher the relative temperature which can be used. As a result, it follows that higher relative temperatures would tend to make the reaction conditions more stringent, while lower temperatures less so. For additional details and explanation of stringency of

hybridization reactions, see Ausubel et al., Current Protocols in Molecular Biology, Wiley Interscience Publishers, (1995).

"Stringent conditions" or "high stringency conditions", as defined herein, may be identified by those that: (1) employ low ionic strength and high temperature for washing, for example 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50°C; (2) employ during hybridization a denaturing agent, such as formamide, for example, 50% (v/v) formamide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50mMsodium phosphate buffer at pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42°C; or (3) employ 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 µg/ml), 0.1% SDS, and 10% dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC (sodium chloride/sodium citrate) and 50% formamide at 55°C, followed by a high-stringency wash consisting of 0.1 x SSC containing EDTA at 55°C.

"Moderately stringent conditions" may be identified as described by Sambrook et al., Molecular Cloning: A Laboratory Manual, New York: Cold Spring Harbor Press, 1989, and include the use of washing solution and hybridization conditions (e.g., temperature, ionic strength and %SDS) less stringent than those described above. An example of moderately stringent conditions is overnight incubation at 37°C in a solution comprising: 20% formamide, 5 x SSC (150 mM NaCl, 15 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5 x Denhardt's solution, 10% dextran sulfate, and 20 mg/ml denatured sheared salmon sperm DNA, followed by washing the filters in 1 x SSC at about 37-50°C. The skilled artisan will recognize how to adjust the temperature, ionic strength, etc. as necessary to accommodate factors such as probe length and the like.

The term "epitope tagged" when used herein refers to a chimeric polypeptide comprising a PRO polypeptide fused to a "tag polypeptide". The tag polypeptide has enough residues to provide an epitope against which an antibody can be made, yet is short enough such that it does not interfere with activity of the polypeptide to which it is fused. The tag polypeptide preferably also is fairly unique so that the antibody does not substantially cross-react with other epitopes. Suitable tag polypeptides generally have at least six amino acid residues and usually between about 8 and 50 amino acid residues (preferably, between about 10 and 20 amino acid residues).

As used herein, the term "immunoadhesin" designates antibody-like molecules which combine the binding specificity of a heterologous protein (an "adhesin") with the effector functions of immunoglobulin constant domains. Structurally, the immunoadhesins comprise a fusion of an amino acid sequence with the desired binding specificity which is other than the antigen recognition and binding site of an antibody (i.e., is "heterologous"), and an immunoglobulin constant domain sequence. The adhesin part of an immunoadhesin molecule typically is a contiguous amino acid sequence comprising at least the binding site of a receptor or a ligand. The immunoglobulin constant domain sequence in the immunoadhesin may be obtained from any immunoglobulin, such as IgG-1, IgG-2, IgG-3, or IgG-4 subtypes, IgA (including IgA-1 and IgA-2), IgE, IgD or IgM.

"Active" or "activity" for the purposes herein refers to form(s) of a PRO polypeptide which retain a biological and/or an immunological activity of native or naturally-occurring PRO, wherein "biological" activity

refers to a biological function (either inhibitory or stimulatory) caused by a native or naturally-occurring PRO other than the ability to induce the production of an antibody against an antigenic epitope possessed by a native or naturally-occurring PRO and an "immunological" activity refers to the ability to induce the production of an antibody against an antigenic epitope possessed by a native or naturally-occurring PRO.

5 The term "antagonist" is used in the broadest sense, and includes any molecule that partially or fully blocks, inhibits, or neutralizes a biological activity of a native PRO polypeptide disclosed herein. In a similar manner, the term "agonist" is used in the broadest sense and includes any molecule that mimics a biological activity of a native PRO polypeptide disclosed herein. Suitable agonist or antagonist molecules specifically include agonist or antagonist antibodies or antibody fragments, fragments or amino acid sequence variants of native PRO polypeptides, peptides, antisense oligonucleotides, small organic molecules, etc. Methods for
10 identifying agonists or antagonists of a PRO polypeptide may comprise contacting a PRO polypeptide with a candidate agonist or antagonist molecule and measuring a detectable change in one or more biological activities normally associated with the PRO polypeptide.

"Treatment" refers to both therapeutic treatment and prophylactic or preventative measures, wherein the object is to prevent or slow down (lessen) the targeted pathologic condition or disorder. Those in need of
15 treatment include those already with the disorder as well as those prone to have the disorder or those in whom the disorder is to be prevented.

"Chronic" administration refers to administration of the agent(s) in a continuous mode as opposed to an acute mode, so as to maintain the initial therapeutic effect (activity) for an extended period of time. "Intermittent" administration is treatment that is not consecutively done without interruption, but rather is cyclic
20 in nature.

"Mammal" for purposes of treatment refers to any animal classified as a mammal, including humans, domestic and farm animals, and zoo, sports, or pet animals, such as dogs, cats, cattle, horses, sheep, pigs, goats, rabbits, etc. Preferably, the mammal is human.

Administration "in combination with" one or more further therapeutic agents includes simultaneous
25 (concurrent) and consecutive administration in any order.

"Carriers" as used herein include pharmaceutically acceptable carriers, excipients, or stabilizers which are nontoxic to the cell or mammal being exposed thereto at the dosages and concentrations employed. Often the physiologically acceptable carrier is an aqueous pH buffered solution. Examples of physiologically acceptable carriers include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptide; proteins, such as serum albumin,
30 gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEEN™, polyethylene glycol (PEG),
35 and PLURONICS™.

"Antibody fragments" comprise a portion of an intact antibody, preferably the antigen binding or variable region of the intact antibody. Examples of antibody fragments include Fab, Fab', F(ab')₂, and Fv

fragments; diabodies; linear antibodies (Zapata et al., *Protein Eng.* 8(10): 1057-1062 [1995]); single-chain antibody molecules; and multispecific antibodies formed from antibody fragments.

Papain digestion of antibodies produces two identical antigen-binding fragments, called "Fab" fragments, each with a single antigen-binding site, and a residual "Fc" fragment, a designation reflecting the ability to crystallize readily. Pepsin treatment yields an $F(ab')_2$ fragment that has two antigen-combining sites and is still capable of cross-linking antigen.

"Fv" is the minimum antibody fragment which contains a complete antigen-recognition and -binding site. This region consists of a dimer of one heavy- and one light-chain variable domain in tight, non-covalent association. It is in this configuration that the three CDRs of each variable domain interact to define an antigen-binding site on the surface of the VH-VL dimer. Collectively, the six CDRs confer antigen-binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding site.

The Fab fragment also contains the constant domain of the light chain and the first constant domain (CH1) of the heavy chain. Fab fragments differ from Fab' fragments by the addition of a few residues at the carboxy terminus of the heavy chain CH1 domain including one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear a free thiol group. $F(ab')_2$ antibody fragments originally were produced as pairs of Fab' fragments which have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

The "light chains" of antibodies (immunoglobulins) from any vertebrate species can be assigned to one of two clearly distinct types, called kappa and lambda, based on the amino acid sequences of their constant domains.

Depending on the amino acid sequence of the constant domain of their heavy chains, immunoglobulins can be assigned to different classes. There are five major classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM, and several of these may be further divided into subclasses (isotypes), e.g., IgG1, IgG2, IgG3, IgG4, IgA, and IgA2.

"Single-chain Fv" or "sFv" antibody fragments comprise the VH and VL domains of antibody, wherein these domains are present in a single polypeptide chain. Preferably, the Fv polypeptide further comprises a polypeptide linker between the VH and VL domains which enables the sFv to form the desired structure for antigen binding. For a review of sFv, see Pluckthun in *The Pharmacology of Monoclonal Antibodies*, vol. 113, Rosenberg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994).

The term "diabodies" refers to small antibody fragments with two antigen-binding sites, which fragments comprise a heavy-chain variable domain (VH) connected to a light-chain variable domain (VL) in the same polypeptide chain (VH - VL). By using a linker that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with the complementary domains of another chain and create two antigen-binding sites. Diabodies are described more fully in, for example, EP 404,097; WO 93/11161; and Hollinger et al., *Proc. Natl. Acad. Sci. USA*, 90:6444-6448 (1993).

An "isolated" antibody is one which has been identified and separated and/or recovered from a

component of its natural environment. Contaminant components of its natural environment are materials which would interfere with diagnostic or therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In preferred embodiments, the antibody will be purified (1) to greater than 95% by weight of antibody as determined by the Lowry method, and most preferably more than 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or nonreducing conditions using Coomassie blue or, preferably, silver stain. Isolated antibody includes the antibody in situ within recombinant cells since at least one component of the antibody's natural environment will not be present. Ordinarily, however, isolated antibody will be prepared by at least one purification step.

The word "label" when used herein refers to a detectable compound or composition which is conjugated directly or indirectly to the antibody so as to generate a "labeled" antibody. The label may be detectable by itself (e.g. radioisotope labels or fluorescent labels) or, in the case of an enzymatic label, may catalyze chemical alteration of a substrate compound or composition which is detectable.

By "solid phase" is meant a non-aqueous matrix to which the antibody of the present invention can adhere. Examples of solid phases encompassed herein include those formed partially or entirely of glass (e.g., controlled pore glass), polysaccharides (e.g., agarose), polyacrylamides, polystyrene, polyvinyl alcohol and silicones. In certain embodiments, depending on the context, the solid phase can comprise the well of an assay plate; in others it is a purification column (e.g., an affinity chromatography column). This term also includes a discontinuous solid phase of discrete particles, such as those described in U.S. Patent No. 4,275,149.

A "liposome" is a small vesicle composed of various types of lipids, phospholipids and/or surfactant which is useful for delivery of a drug (such as a PRO polypeptide or antibody thereto) to a mammal. The components of the liposome are commonly arranged in a bilayer formation, similar to the lipid arrangement of biological membranes.

A "small molecule" is defined herein to have a molecular weight below about 500 Daltons.

25 II. Compositions and Methods of the Invention

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO polypeptides. In particular, cDNAs encoding various PRO polypeptides have been identified and isolated, as disclosed in further detail in the Examples below. It is noted that proteins produced in separate expression rounds may be given different PRO numbers but the UNQ number is unique for any given DNA and the encoded protein, and will not be changed. However, for sake of simplicity, in the present specification the protein encoded by the full length native nucleic acid molecules disclosed herein as well as all further native homologues and variants included in the foregoing definition of PRO, will be referred to as "PRO/number", regardless of their origin or mode of preparation.

As disclosed in the Examples below, various cDNA clones have been deposited with the ATCC. The actual nucleotide sequences of those clones can readily be determined by the skilled artisan by sequencing of the deposited clone using routine methods in the art. The predicted amino acid sequence can be determined from the nucleotide sequence using routine skill. For the PRO polypeptides and encoding nucleic acids described

herein, Applicants have identified what is believed to be the reading frame best identifiable with the sequence information available at the time.

A. Full-Length PRO Polypeptides

1. PRO1560

5 Using the WU-BLAST2 sequence alignment computer program, the full-length native sequence PRO1560 (shown in Figure 2 and SEQ ID NO:4) has certain amino acid sequence identity with Tspan-6, identified after the discovery of the present invention herein. Accordingly, it is presently believed that PRO1560 disclosed in the present application is a newly identified member of the tetraspan family.

10 2. PRO444

The DNA26846-1397 clone was isolated from a human fetal lung library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA26846-1397 clone encodes a secreted factor. As far as is known, the DNA26846-1397 sequence encodes a novel factor designated herein as PRO444. Using the WU-BLAST2 sequence alignment computer program, no significant sequence identity
15 with known proteins was revealed.

3. PRO1018

The DNA56107-1415 clone was isolated from a human ovary tumor tissue library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. As far as is known, the
20 DNA56107-1415 sequence encodes a novel factor designated herein as PRO1018; using the WU-BLAST2 sequence alignment computer program, no significant sequence identities to any known proteins were revealed.

4. PRO1773

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the
25 full-length native sequence PRO1773 (shown in Figure 8 and SEQ ID NO:10) has certain amino acid sequence identity with a portion of the retinol dehydrogenase type II protein of rattus norvegicus (ROH2_RAT). Accordingly, it is presently believed that PRO1773 disclosed in the present application is a newly identified member of the retinol dehydrogenase protein family and may possess activity typical of that protein family.

30 5. PRO1477

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1477 (shown in Figure 10 and SEQ ID NO:12) has certain amino acid sequence identity with the mannosyl-oligosaccharide 1,2-alpha-mannosidase protein (A54408). Accordingly, it is presently
35 believed that PRO1477 disclosed in the present application is a newly identified member of the mannosidase protein family and may possess activity typical of the mannosidase protein family.

6. PRO1478

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1478 (shown in Figure 12 and SEQ ID NO:17) has certain amino acid sequence identity with galactosyltransferases. Accordingly, it is presently believed that PRO1478 disclosed in the present application is a newly identified member of the galactosyltransferase family and may possess at least one shared mechanism with other members of this family.

7. PRO831

The DNA56862-1343 clone was isolated from a human uterus library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA56862-1343 clone does encode a secreted factor. As far as is known, the DNA56862-1343 sequence encodes a novel factor designated herein as PRO831; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

8. PRO1113

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1113 (shown in Figure 16 and SEQ ID NO:24) has certain amino acid sequence identity with LIG-1 and SLIT. Accordingly, it is presently believed that PRO1113 disclosed in the present application is a newly identified member of the leucine rich repeat family and may possess protein-protein interaction activity as is typical of this family.

9. PRO1194

As far as is known, the DNA57841-1522 sequence encodes a novel factor designated herein as PRO1194; using WU-BLAST2 sequence alignment computer programs, limited sequence identities to known proteins were revealed.

10. PRO1110

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1110 (shown in Figure 20 and SEQ ID NO:31) has certain amino acid sequence identity with the murine myeloid upregulated protein. Accordingly, it is presently believed that PRO1110 disclosed in the present application is a newly identified member of the myeloid upregulated protein family and may possess activity typical of that family.

11. PRO1378

The DNA58730-1607 clone was isolated from a bone marrow library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA58730-1607 clone encodes a secreted factor. As far as is known, the DNA58730-1607 sequence encodes a novel factor designated herein as PRO1378. WU-BLAST2 sequence alignment computer programs revealed some sequence identities between

the amino acid sequence of PRO1378 with known proteins. However, they were determined to not be significant.

12. PRO1481

As far as is known, the DNA58732-1650 sequence encodes a novel factor designated herein as PRO1481. Using WU-BLAST2 sequence alignment computer programs, only some sequence identities to known proteins were revealed.

13. PRO1189

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1189 (shown in Figure 26 and SEQ ID NO:43) has certain amino acid sequence identity with the amino acid sequence of an E25 protein designated "MUSE25A_1" in the Dayhoff database. Accordingly, it is presently believed that PRO1189 disclosed in the present application is a newly identified member of the E25 protein family and may possess activity or properties typical of that family.

15 14. PRO1415

The DNA58852-1637 clone was isolated from a diseased human prostate tissue library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. As far as is known, the DNA58852-1637 sequence encodes a novel factor designated herein as PRO1415; using the WU-BLAST2 sequence alignment computer program, no significant sequence identities to any known proteins were revealed.

20 15. PRO1411

As far as is known, the DNA59212-1627 sequence encodes a novel factor designated herein as PRO1411. However, using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

25 16. PRO1295

As far as is known, the DNA59218-1559 sequence encodes a novel factor designated herein as PRO1295. Using WU-BLAST2 sequence alignment computer programs, only some sequence identities to known proteins were revealed.

30 17. PRO1359

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1359 (shown in Figure 34 and SEQ ID NO:56) has certain amino acid sequence identity with N-acetylgalactosamine alpha-2, 6-sialyltransferase. Accordingly, it is presently believed that PRO1359 disclosed in the present application is a newly identified member of the sialyltransferase family and may possess transferase activity typical of this family.

18. PRO1190

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1190 (shown in Figure 36 and SEQ ID NO:58) has certain amino acid sequence identity with both rat and human CDO. Accordingly, it is presently believed that PRO1190 disclosed in the present application is a newly identified member of the CDO family and may possess cell adhesion activity typical of the CDO family.

19. PRO1772

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1772 (shown in Figure 38 and SEQ ID NO:63) has certain amino acid sequence identity with a human microsomal dipeptidase protein (P_R13857). Accordingly, it is presently believed that PRO1772 disclosed in the present application is a newly identified member of the peptidase protein family and may possess activity typical of that protein family.

20. PRO1248

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1248 (shown in Figure 40 and SEQ ID NO:68) has amino acid sequence identity with the PUT-2 protein (AF026198_5). Accordingly, it is presently believed that PRO1248 disclosed in the present application is a newly PUT-2 homolog and may possess activity typical of the PUT-2 protein.

20 21. PRO1316

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1316 (shown in Figure 42 and SEQ ID NO:70) has certain amino acid sequence identity with murine dickkopf. Accordingly, it is presently believed that PRO1316 disclosed in the present application is a newly identified member of the dickkopf family and may possess the ability to cause head induction from the Spemann organizer and/or Wnt antagonism.

22. PRO1197

As far as is known, the DNA60611-1524 sequence encodes a novel factor designated herein as PRO1197. Using WU-BLAST2 sequence alignment computer programs, only some sequence identities to known proteins were revealed as further described in the examples.

23. PRO1293

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1293 (shown in Figure 46 and SEQ ID NO:77) has certain amino acid sequence identity with the human Ig heavy chain V region protein (HSVCD54_1). Accordingly, it is presently believed that PRO1293 disclosed in the present application is a newly identified member of the Ig superfamily of proteins and fragments thereof and may possess activity typical of that family.

24. PRO1380

The DNA60740-1615 clone was isolated from a human retina library. As far as is known, the DNA60740-1615 sequence encodes a novel multi-span transmembrane polypeptide designated herein as PRO1380. Using WU-BLAST2 sequence alignment computer programs, some sequence identity with known proteins were revealed.

5

25. PRO1265

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1265 (shown in Figure 50 and SEQ ID NO:84) has certain amino acid sequence identity with the Fig1 polypeptide designated "MMU70429_1" in the Dayhoff database (version 35.45 SwissProt 35). Accordingly, it is presently believed that PRO1265 disclosed in the present application is a newly identified member of the FIG1 family and may possess activity typical of the FIG1 polypeptide, including activation by interleukin-4.

10

26. PRO1250

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1250 (shown in Figure 52 and SEQ ID NO:86) has certain amino acid sequence identity with the human long chain fatty acid CoA ligase protein (LCFB_HUMAN). Accordingly, it is presently believed that PRO1250 disclosed in the present application is a newly identified long chain fatty acid CoA ligase homolog that may have activity typical of long chain fatty acids CoA ligase.

15

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27. PRO1475

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1475 (shown in Figure 54 and SEQ ID NO:88) has certain amino acid sequence identity with a portion of the mouse alpha-3-D-mannoside 6-phosphate 1,2-N-acetylglucosaminyltransferase I protein. Accordingly, it is presently believed that PRO1475 disclosed in the present application is a newly identified member of the N-acetylglucosaminyltransferase protein family and may possess activity typical of that protein family.

25

28. PRO1377

As described herein, WU-BLAST2 sequence alignment computer programs were used to determine the sequence identity of the PRO1377 amino acid sequence with the amino acid sequences of known proteins. While some sequence identities were revealed, they were determined to not be significant. Accordingly, as far as is known, the DNA61608 sequence encodes a novel transmembrane protein designated herein as PRO1377.

30

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29. PRO1326

The DNA62808-1582 clone is believed to encode a secreted factor. As far as is known, the DNA62808-1582 sequence encodes a novel factor designated herein as PRO1326; using WU-BLAST2 sequence alignment

computer programs, sequence identities to known proteins were revealed but determined not to be significant.

30. PRO1249

The DNA62809-1531 clone was isolated from a human colon tumor tissue library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. As far as is known, the DNA62809-1531 sequence encodes a novel factor designated herein as PRO1249; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

31. PRO1315

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1315 (shown in Figure 62 and SEQ ID NO:104) has certain amino acid sequence identity with the class II cytokine receptor 4 protein of mus musculus (MMU53696_1). Accordingly, it is presently believed that PRO1315 disclosed in the present application is a newly identified member of the cytokine receptor protein family and may possess activity typical of that family.

15 32. PRO1599

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1599 (shown in Figure 64 and SEQ ID NO:111) has certain amino acid sequence identity with Dayhoff sequence "CFAD_PIG". Accordingly, it is presently believed that PRO1599 disclosed in the present application is a newly identified member of the Granzyme M family and may possess activity or properties typical of the Granzyme M family.

33. PRO1430

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1430 (shown in Figure 66 and SEQ ID NO:116) has certain amino acid sequence identity prostate specific reductase (designated "P_W03198" in the Dayhoff database). Accordingly, it is presently believed that PRO1430 disclosed in the present application is a newly identified member of the reductase family and may possess activity typical of members of the reductase family.

34. PRO1374

As far as is known, the DNA64849-1604 sequence encodes a novel factor designated herein as PRO1374; using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins such as the human alpha subunit of P4HA were revealed. Therefore, it is believed that PRO1374 is related to P4HA and may share one or more mechanisms.

35 35. PRO1311

The DNA64863-1573 clone was isolated from human aortic endothelial cells and is believed to encode a novel transmembrane polypeptide designated herein as PRO1311. Using WU-BLAST2 sequence alignment

computer programs, some sequence identities with known proteins were revealed, but were determined to not be significant.

36. PRO1357

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1357 (shown in Figure 72 and SEQ ID NO:128) has certain amino acid sequence identity with the von Ebner minor salivary gland protein of mus musculus (MMU46068_1). Accordingly, it is presently believed that PRO1357 disclosed in the present application is a newly identified von Ebner minor salivary gland protein homolog.

10 37. PRO1244

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1244 (shown in Figure 74 and SEQ ID NO:130) has certain amino acid sequence identity with a known implantation-associated protein designated "AF008554_1" on the Dayhoff database (version 35.45 SwissProt 35). Accordingly, it is presently believed that PRO1244 disclosed in the present application is a newly identified member of the implantation-associated protein family and may possess attachment activity typical of that protein family.

38. PRO1246

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1246 (shown in Figure 76 and SEQ ID NO:132) has certain amino acid sequence identity with the murine bone-related sulphatase-like precursor protein (P_R51355). Accordingly, it is presently believed that PRO1246 disclosed in the present application is a newly identified bone-related sulphatase homolog and may possess activity typical of bone-related sulfatase.

25 39. PRO1356

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1356 (shown in Figure 78 and SEQ ID NO:134) has certain amino acid sequence identity with the CPE-receptor protein of mus musculus (AB000713_1). Accordingly, it is presently believed that PRO1356 disclosed in the present application is a newly identified member of the CPE receptor family and may possess activity typical of that family.

40. PRO1275

As far as is known, the DNA64888-1542 sequence encodes a novel factor designated herein as PRO1275. Using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

41. PRO1274

As far as is known, the DNA64889-1541 sequence encodes a novel factor designated herein as PRO1274. Using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

5 42. PRO1412

The DNA64897-1628 clone is believed to be a secreted factor. As far as is known, the DNA64897-1628 sequence encodes a novel factor designated herein as PRO1412; using WU-BLAST2 sequence alignment computer programs, sequence identities to known proteins were revealed but determined not to be significant.

10 43. PRO1557

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1557 (shown in Figure 86; SEQ ID NO:142) has certain amino acid sequence identity chordin protein designated AF034606_1 in the Dayhoff database. Accordingly, it is presently believed that PRO1557 disclosed in the present application is a newly identified member of the chordin family and may possess activity
15 typical of the chordin family.

44. PRO1286

The DNA64903-1553 clone identified using techniques which selects for nucleotide sequences encoding secreted proteins. As far as is known, the DNA64903 sequence encodes a novel secreted factor designated herein
20 as PRO1286. Using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed; however, it was determined that they were not significant.

45. PRO1294

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length
25 native sequence PRO1294 (shown in Figure 90 and SEQ ID NO:146) has certain amino acid sequence identity with the neuronal olfactomedin-related ER localized protein of the rat (I73636). Accordingly, it is presently believed that PRO1294 disclosed in the present application is a newly identified olfactomedin homolog and may possess activity typical of that protein.

30 46. PRO1347

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1347 (shown in Figure 92 and SEQ ID NO:148) has certain amino acid sequence identity with butyrophilin. Moreover, there is a transmembrane domain approximately in the middle of the sequence as is typical of butyrophilins. Accordingly, it is presently believed that PRO1347 disclosed in the present application
35 is a newly identified member of the butyrophilin family and may play a role in the budding and release of milk-fat globules during lactation.

47. PRO1305

The DNA64952-1568 clone was isolated from a human fetal kidney library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA64952-1568 clone does encode a secreted factor. As far as is known, the DNA64952-1568 sequence encodes a novel factor designated herein as PRO1305; using the WU-BLAST2 sequence alignment computer program, no sequence identities to
5 any known proteins were revealed.

48. PRO1273

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1273 (shown in Figure 96 and SEQ ID NO:158) has certain amino acid sequence identity with a
10 lipocalin precursor. Moreover, Figure 96 shows that PRO1273 has a motif conserved in lipocalins. Accordingly, it is presently believed that PRO1273 disclosed in the present application is a newly identified member of the lipocalin family and shares at least one mechanism with lipocalins.

49. PRO1302

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1302 (shown in Figure 98 and SEQ ID NO:160) has certain amino acid sequence identity with CD33L1 and CD33L2. Accordingly, it is presently believed that PRO1302 disclosed in the present application is a newly identified member of the sialoadhesin family and possesses characteristics typical of this family. Specifically, PRO1302 may be involved in cancer, inflammation, hemopoiesis, neuronal development and/or
15 immunity.
20

50. PRO1283

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1283 (shown in Figure 100 and SEQ ID NO:162) has certain amino acid sequence identity
25 with the rat odorant binding protein homolog OBP-II precursor (A40464). Accordingly, it is presently believed that PRO1283 disclosed in the present application is a newly odorant binding protein and may possess activity typical of the odorant binding proteins.

51. PRO1279

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1279 (shown in Figure 102 and SEQ ID NO:170) has certain amino acid sequence identity
30 with the mouse neuropsin protein (I56559). Accordingly, it is presently believed that PRO1279 disclosed in the present application is a newly identified neuropsin homolog and may possess activity typical of the neuropsin protein.

35

52. PRO1304

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length

native sequence PRO1304 (shown in Figure 104 and SEQ ID NO:180) has certain amino acid sequence identity with the FK-506 binding protein of mus musculus (AF040252_1). Accordingly, it is presently believed that PRO1304 disclosed in the present application is a newly identified member of the FK506 binding protein family and may possess activity typical of that family.

5 53. PRO1317

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1317 (shown in Figure 106 and SEQ ID NO:189) has certain amino acid sequence identity with human CD97 protein. Accordingly, it is presently believed that PRO1317 disclosed in the present application is a leukocyte antigen that may be involved in leukocyte activation.

10

54. PRO1303

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1303 (shown in Figure 108 and SEQ ID NO:194) has certain amino acid sequence identity with neuropsin. Accordingly, it is presently believed that PRO1303 disclosed in the present application is a newly identified member of the serine protease family and may possess catabolic activity typical of this family.

15

55. PRO1306

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1306 (shown in Figure 110 and SEQ ID NO:196) has certain amino acid sequence identity with Dayhoff sequence no. AIF1_HUMAN. Accordingly, it is presently believed that PRO1306 disclosed in the present application is a newly identified member of the AIF1/daintain family and may possess activity and properties typical of AIF1/daintain.

20

56. PRO1336

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1336 (shown in Figure 112 and SEQ ID NO:198) has certain amino acid sequence identity with slit. Accordingly, it is presently believed that PRO1336 disclosed in the present application is a newly identified member of the EGF-repeat family and may possess protein interaction mediation activity.

25

30 57. PRO1278

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1278 (shown in Figure 114 and SEQ ID NO:203) has certain amino acid sequence identity lysozyme c -1 precursor designated "LYC1_ANAPL" in the Dayhoff database. Accordingly, it is presently believed that PRO1278 disclosed in the present application is a newly identified member of the lysozyme family and may possess hydrolytic and other activity typical of the lysozyme family.

35

58. PRO1298

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1298 (shown in Figure 116 and SEQ ID NO:210) has certain amino acid sequence identity with glycosyltransferase alg2. Accordingly, it is presently believed that PRO1298 disclosed in the present application is a newly identified member of the glycosyltransferase family and may share at least one mechanism with members of this family.

59. PRO1301

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1301 (shown in Figure 118 and SEQ ID NO:212) has consistent amino acid sequence identity with cytochrome P450 proteins. Accordingly, it is presently believed that PRO1301 disclosed in the present application is a newly identified member of the cytochrome P450 family and may possess monooxygenase activity typical of the cytochrome P450 family.

60. PRO1268

As far as is known, the DNA66519-1535 sequence encodes a novel transmembrane polypeptide factor designated herein as PRO1268. Using WU-BLAST2 sequence alignment computer programs, sequence identity to a known protein was revealed, but determined to not be significant.

61. PRO1269

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1269 (shown in Figure 122 and SEQ ID NO:216) has certain amino acid sequence identity a bovine granulocyte peptide A precursor, designated "P_W23722" on the Dayhoff database (version 35.45 SwissProt 35). Accordingly, it is presently believed that PRO1269 disclosed in the present application is a newly identified member of the granulocyte A peptide family and may possess microbial activity typical of that family of peptides.

62. PRO1327

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1327 (shown in Figure 124 and SEQ ID NO:218) has certain amino acid sequence identity with the rat neurexophilin-1 protein (NPH1_RAT). Accordingly, it is presently believed that PRO1327 disclosed in the present application is a newly identified member of the neurexophilin protein family and may possess activity typical of that protein family.

63. PRO1382

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1382 (shown in Figure 126 and SEQ ID NO:220) has certain amino acid sequence identity with the amino acid sequence of a known cerebellin-like glycoprotein designated "CERL_RAT" in the Dayhoff

database. Accordingly, it is presently believed that PRO1382 disclosed in the present application is a newly identified member of the cerebellin family of neuropeptides and may possess activity and properties typical of cerebellin.

64. **PRO1328**

5 The DNA66658-1584 clone was isolated from a human diseased prostate tissue library using a trapping technique which selects for nucleotide sequences encoding proteins. As far as is known, the DNA66658-1584 sequence encodes a novel factor designated herein as PRO1328; using the WU-BLAST2 sequence alignment computer program, no significant sequence identities to any known proteins were revealed.

10 65. **PRO1325**

The DNA66659-1593 clone was isolated from a human thymus tissue library using a trapping technique which selects for nucleotide sequences encoding proteins. As far as is known, the DNA66659-1593 sequence encodes a novel factor designated herein as PRO1325; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

15

66. **PRO1340**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1340 (shown in Figure 132 and SEQ ID NO:229) has certain amino acid sequence identity with Dayhoff sequence no. I46536. Accordingly, it is presently believed that PRO1340 disclosed in the present
20 application is a newly identified member of the cadherin family and may possess activity and properties typical of the cadherin family.

67. **PRO1339**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native
25 sequence PRO1339 (shown in Figure 134 and SEQ ID NO:234) has certain amino acid sequence identity with human pancreatic carboxypeptidase and carboxypeptidase a1. Accordingly, it is presently believed that PRO1339 disclosed in the present application is a newly identified member of the carboxypeptidase family and possesses caboxypeptidase activity.

30 68. **PRO1337**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1337 (shown in Figure 136 and SEQ ID NO:236) has certain amino acid sequence identity with a human TBG identified as "THBG_HUMAN" in the Dayhoff database. Accordingly, it is presently believed that PRO1337 disclosed in the present application is a newly identified member of the TBG family and may
35 possess thyroid hormone transport capability and have other

69. PRO1342

The DNA66674-1599 clone was isolated from human esophageal tissue. As described in further detail below, using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed. The DNA66674-1599 clone appears to encode for a novel transmembrane polypeptide.

5 70. PRO1343

The DNA66675-1587 clone was isolated from a human smooth muscle cell tissue library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA66675-1587 clone does encode a secreted factor. As far as is known, the DNA66675-1587 sequence encodes a novel factor designated herein as PRO1343; using the WU-BLAST2 sequence alignment computer program, no
10 significant sequence identities to any known proteins were revealed.

71. PRO1480

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1480 (shown in Figure 142 and SEQ ID NO:253) has certain amino acid sequence identity with
15 Dayhoff sequence no. I48746. Accordingly, it is presently believed that PRO1480 disclosed in the present application is a newly identified member of the Semaphorin C family

72. PRO1487

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native
20 sequence PRO1487 (Figure 144; SEQ ID NO:260) has certain amino acid sequence identity with a radical fringe protein designated GGU82088_1 on the Dayhoff database. Accordingly, it is presently believed that PRO1487 disclosed in the present application is a newly identified member of the fringe family and may possess activity typical of the fringe family.

25 73. PRO1418

As far as is known, the DNA68864-1629 sequence encodes a novel factor designated herein as PRO1418. Using WU-BLAST2 sequence alignment computer programs, sequence identities to known proteins were minimal.

30 74. PRO1472

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1472 (shown in Figure 148 and SEQ ID NO:267) has certain amino acid sequence identity with butyrophilin. Accordingly, it is presently believed that PRO1472 disclosed in the present application is a newly
35 identified member of the butyrophilin family and may possess involvement in lactation.

75. PRO1461

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native

sequence PRO1461 (shown in Figure 150 and SEQ ID NO:269) has certain amino acid sequence identity the trypsin-like enzyme identified as "P_R89435" on the Dayhoff database. Accordingly, it is presently believed that PRO1461 disclosed in the present application is a newly identified member of the serine protease family and may possess serine protease activity, and more particularly, may possess enzymatic activity typical of other trypsin-like enzymes. Homology was also found to exist between the PRO1461 amino acid sequence and other
5 trypsin-like enzymes and serine proteases in the Dayhoff database.

76. PRO1410

The DNA68874-1622 clone was isolated from a human brain meningioma tissue library using a trapping technique which selects for nucleotide sequences encoding proteins. As far as is known, the DNA68874-1622
10 sequence encodes a novel factor designated herein as PRO1410; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

77. PRO1568

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native
15 sequence PRO1568 (shown in Figure 154 and SEQ ID NO:273) has certain amino acid sequence identity to tetraspan 5 and tetraspan 4. Accordingly, it is presently believed that PRO1568 disclosed in the present application is a newly identified member of the tetraspanin family and may possess molecular facilitator activity typical of this family.

20 78. PRO1570

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1570 (shown in Figure 156 and SEQ ID NO:275) has certain amino acid sequence identity with SP60; however, for the first time, the first 199 amino acids (or amino terminal end) of that protein are identified and presented herein. Accordingly, it is presently believed that PRO1570 disclosed in the present application
25 is a newly identified member of the serine protease family and is involved in carcinoma.

79. PRO1317

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1317 (shown in Figure 158 and SEQ ID NO:277) has certain amino acid sequence identity with
30 a known semaphorin B protein, designated "I48745" on the Dayhoff database. Accordingly, it is presently believed that PRO1317 disclosed in the present application is a newly identified member of the semaphorin glycoprotein family and may possess activity or properties typical of semaphorins.

80. PRO1780

35 Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1780 (shown in Figure 160 and SEQ ID NO:282) has certain amino acid sequence identity with a known glucuronosyltransferase designated "UDA2_RABIT" in the Dayhoff database. Accordingly, it is

presently believed that PRO1780 disclosed in the present application is a newly identified member of the glucuronosyltransferase family and may possess enzymatic activity and other properties typical of the glucuronosyltransferase family.

81. PRO1486

5 Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1486 (shown in Figure 162 and SEQ ID NO:287) has certain amino acid sequence identity with cerebellin 1 precursor. Accordingly, it is presently believed that PRO1486 disclosed in the present application is a newly identified member of the cerebellin family and shares at least one mechanism with cerebellin.

10 82. PRO1433

The DNA71184-1634 clone was isolated from a human adrenal gland tissue library using a trapping technique which selects for nucleotide sequences encoding proteins. As far as is known, the DNA71184-1634 sequence encodes a novel factor designated herein as PRO1433; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

15

83. PRO1490

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1490 (shown in Figure 166 and SEQ ID NO:297) has certain amino acid sequence identity with a portion of the 1-acyl-sn-glycerol-3-phosphate acyltransferase protein (S60478).
20 Accordingly, it is presently believed that PRO1490 disclosed in the present application is a newly identified member of the acyltransferase protein family and may possess activity typical of 1-acyl-sn-glycerol-3-phosphate acyltransferase proteins.

84. PRO1482

25 The DNA71234-1651 clone was isolated from a human adrenal gland library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA71234-1651 clone does encode a secreted factor. As far as is known, the DNA71234-1651 sequence encodes a novel factor designated herein as PRO1482; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

30

85. PRO1446

As far as is known, the DNA71277-1636 sequence encodes a novel factor designated herein as PRO1446. Using WU-BLAST2 sequence alignment computer programs, minimal sequence identities to known proteins were revealed.

35

86. PRO1558

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length

native sequence PRO1558 (shown in Figure 172 and SEQ ID NO:306) has significant amino acid sequence identity with a methyltransferase protein (CAMT_EUCGU). Accordingly, it is presently believed that PRO1558 disclosed in the present application is a newly identified member of the methyltransferase protein family and may possess activity typical of that protein family.

5 87. PRO1604

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1604 (shown in Figure 174 and SEQ ID NO:308) has certain amino acid sequence identity with the mouse liver cancer-originated cell growth factor designated P_W37483 on the Dayhoff database. Accordingly, it is presently believed that PRO1604 disclosed in the present application is a newly identified member of the HDGF family and may possess growth factor activity typical of other HDGFs.

88. PRO1491

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1491 (shown in Figure 176 and SEQ ID NO:310) has certain amino acid sequence identity with a portion of the collapsin-2 protein of Gallus gallus (GGU28240_1). Accordingly, it is presently believed that PRO1491 disclosed in the present application is a newly identified member of the collapsin protein family and may possess activity typical of that protein family.

89. PRO1431

It has been found that the full-length native sequence PRO1431 [shown in Figure 178 (SEQ ID NO:315) has significant sequence identity with the SH3 domain containing protein SH17_HUMAN. Accordingly, it is presently believed that PRO1431 disclosed in the present application is a newly identified member of proteins having an SH3 domains and may possess signal transduction properties.

25 90. PRO1563

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of a full-length native sequence PRO1563 (shown in Figure 180 and SEQ ID NO:317) has certain amino acid sequence identity with a portion of the mouse ADAMTS-1 protein (AB001735_1). Accordingly, it is presently believed that PRO1563 disclosed in the present application is a newly identified member of the ADAM protein family and may possess activity typical of that protein family.

91. PRO1565

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1565 (shown in Figure 182 and SEQ ID NO:322) has certain amino acid sequence identity with a portion of the chondromodulin-I protein of rattus norvegicus (AF051425_1). Accordingly, it is presently believed that PRO1565 disclosed in the present application is a newly identified member of the chondromodulin protein family and may possess activity typical of that protein family.

92. PRO1571

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1571 (shown in Figure 184 and SEQ ID NO:324) has certain amino acid sequence identity with a portion of the human clostridium perfringens enterotoxin receptor protein (AB000712_1). Accordingly, it is presently believed that PRO1571 disclosed in the present application is a newly identified CPE-R homolog and may possess activity typical of the CPE-R protein.

93. PRO1572

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1572 (shown in Figure 186 and SEQ ID NO:326) has certain amino acid sequence identity with CPE-R. Accordingly, it is presently believed that PRO1572 disclosed in the present application is related to CPE-R and may possess at least one shared mechanism.

94. PRO1573

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1573 (shown in Figure 188 and SEQ ID NO:328) has certain amino acid sequence identity with CPE-R. Accordingly, it is presently believed that PRO1573 disclosed in the present application is related to CPE-R and may possess at least one shared mechanism.

95. PRO1488

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1488 (Figure 190; SEQ ID NO:330) has certain amino acid sequence identity with a known CPE-R designated "AB000712_1" on the Dayhoff database. Accordingly, it is presently believed that PRO1488 disclosed in the present application is a newly identified member of the CPE-R family and may possess binding activity typical of the CPE-R family.

96. PRO1489

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1489 (shown in Figure 192 and SEQ ID NO:332) has certain amino acid sequence identity with the clostridium perfringens enterotoxin receptor of Cercopithecus aethiops (D88492_1). Accordingly, it is presently believed that PRO1489 disclosed in the present application is a newly identified clostridium perfringens enterotoxin receptor homolog and may possess activity typical of the clostridium perfringens enterotoxin receptor protein.

97. PRO1474

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1474 (shown in Figure 194 and SEQ ID NO:334) has certain amino acid sequence identity with ovomucoid. Accordingly, it is presently believed that PRO1474 disclosed in the present application is a newly

identified member of the kazal serine protease inhibitor family and may possess serine protease inhibitory activity typical of this family.

98. PRO1508

5 The DNA73742-1508 clone was isolated from a human diseased cartilage tissue library. As far as is known, the DNA73742-1508 sequence encodes a novel factor designated herein as PRO1508; although, using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

99. PRO1555

10 The DNA73744-1665 clone was isolated from a human tissue library. As far as is known, the DNA73744 sequence encodes a novel transmembrane protein designated herein as PRO1555. Using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

100. PRO1485

15 Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1485 (shown in Figure 200 and SEQ ID NO:340) has certain amino acid sequence identity with lysozyme C precursor peptide. Accordingly, it is presently believed that PRO1485 disclosed in the present application is a newly identified member of the lysozyme family and shares at least one like mechanism.

20 101. PRO1564

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of a full-length native sequence PRO1564 (shown in Figure 202 and SEQ ID NO:347) has certain amino acid sequence identity with a portion of a mouse polypeptide GalNAc transferase T4 protein (MMU73819_1). Accordingly, it is presently believed that PRO1564 disclosed in the present application is a newly identified
25 member of the N-acetylgalactosaminyltransferase protein family and may possess activity typical of that protein family.

102. PRO1755

30 As far as is known, the DNA76396-1698 sequence encodes a novel transmembrane protein designated herein as PRO1755. Although, some sequence identities to known proteins was revealed using WU-BLAST2 sequence alignment computer programs.

103. PRO1757

35 The DNA76398-1699 clone was isolated from a human testicular tissue library using a trapping technique which selects for nucleotide sequences encoding proteins. As far as is known, the DNA76398-1699 sequence encodes a novel factor designated herein as PRO1757; using the WU-BLAST2 sequence alignment computer program, no significant sequence identities to any known proteins were revealed.

104. PRO1758

The DNA76399-1700 clone was isolated from a library derived from human thymus tissue obtained from a fetus that died at 17 weeks' gestation from anencephalus. It is believed that the DNA76399-1700 clone encodes a novel secreted factor, designated herein as PRO1758. Using WU-BLAST2 sequence alignment computer programs, significant sequence identity was revealed between the amino acid sequences of PRO1758 and Dayhoff sequence No. AC005328_2.

105. PRO1575

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1575 (shown in Figure 210 and SEQ ID NO:358) has certain amino acid sequence identity with Dayhoff sequence no. A12005_1. Accordingly, it is presently believed that PRO1575 disclosed in the present application is a newly identified member of the protein disulfide isomerase family and may possess activity and properties typical of the disulfide isomerase family.

106. PRO1787

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1787 (shown in Figure 212 and SEQ ID NO:364) has certain amino acid sequence identity with various species of myelin p0. Accordingly, it is presently believed that PRO1787 disclosed in the present application is a newly identified member of the myelin p0 protein family and may share at least one similar mechanism. It is believed that modulators of PRO1787 may be used to treat myelin p0 associated disorders, such as neuropathy, hereditary tooth disease, etc.

107. PRO1781

Using WU-BLAST2 sequence alignment computer programs, some sequence identities were found between the PRO1781 amino acid sequence (SEQ ID NO:366) and the amino acid sequences of known proteins, but were not found to be significant. Accordingly, as far as is known, the DNA76522-2500 sequence encodes a novel protein.

108. PRO1556

The DNA76529-1666 clone was isolated from a human breast tumor tissue library. As far as is known, the DNA76529-1666 sequence encodes a novel transmembrane protein designated herein as PRO1556. Using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

109. PRO1759

As far as is known, the DNA76531-1701 sequence encodes a novel factor designated herein as PRO1759; using WU-BLAST2 sequence alignment computer programs, limited sequence identities to known proteins were revealed.

110. PRO1760

As far as is known, the DNA76532-1702 sequence encodes a novel factor designated herein as PRO1760; using WU-BLAST2 sequence alignment computer programs, limited sequence identities to known proteins were revealed.

5 111. PRO1561

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of a full-length native sequence PRO1561 (shown in Figure 222 and SEQ ID NO:378) has certain amino acid sequence identity with a portion of the human phospholipase A2 protein (P_R63053). Accordingly, it is presently believed that PRO1561 disclosed in the present application is a newly identified member of the
10 phospholipase A2 protein family and may possess activity typical of that protein family.

112. PRO1567

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1567 (Figure 224; SEQ ID NO:383) has certain amino acid sequence identity with human colon
15 specific gene CSG6 polypeptide, identified as P_W06549 on the Dayhoff database. Accordingly, it is presently believed that PRO1567 disclosed in the present application is a newly identified CSG expression product, and may possess properties typical of such proteins.

113. PRO1693

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1693 (shown in Figure 226 and SEQ ID NO:385) has certain amino acid sequence identity with a portion of a mouse insulin-like growth factor binding protein (ALS_MOUSE).
20 Accordingly, it is presently believed that PRO1693 disclosed in the present application is a newly identified member of the insulin-like growth factor binding protein family and may possess activity typical of that protein
25 family.

114. PRO1784

As far as is known, the DNA77303-2502 sequence encodes a novel factor designated herein as PRO1784; using WU-BLAST2 sequence alignment computer programs, some sequence identities to known
30 proteins were revealed.

115. PRO1605

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1605 (shown in Figure 230 and SEQ ID NO:395) has certain amino acid
35 sequence identity with a portion of the human alpha-1,3-mannosylglycoprotein beta-1,6-n-acetyltransferase protein (GNT5_HUMAN). Accordingly, it is presently believed that PRO1605 disclosed in the present application is a newly identified member of the glycosyltransferase protein family and may possess activity

typical of that protein family.

116. **PRO1788**

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1788 (shown in Figure 232 and SEQ ID NO:397) has certain amino acid sequence identity with
5 Dayhoff sequence "GARP_HUMAN", a leucine-rich repeat-containing protein encoded by a gene localized in the 11q14 chromosomal region. Accordingly, it is presently believed that PRO1788 disclosed in the present application is a newly identified member of the leucine-rich repeat-containing family and may possess activity or properties typical of the leucine-rich repeat-containing family.

10 117. **PRO1801**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1801 (shown in Figure 234 and SEQ ID NO:402) has certain amino acid sequence identity with a portion of the IL-19 protein (P_W37935). Accordingly, it is presently believed that PRO1801 disclosed in the present application is a newly identified member of the IL-10-related cytokine family
15 and may possess activity typical of that cytokine family.

118. **UCP4**

Using the Megalign DNASTAR computer program (and algorithms and parameters in this software set by the manufacturer) (Oxford Molecular Group, Inc.), it has been found that a full-length native sequence UCP4
20 (shown in Figure 236 and SEQ ID NO:406) has certain amino acid sequence identity with UCP3, UCP2 and UCP1. Accordingly, it is presently believed that UCP4 disclosed in the present application is a newly identified member of the human uncoupling protein family and may possess activity(s) and/or property(s) typical of that protein family, such as the ability to enhance or suppress metabolic rate by affecting mitochondrial membrane potential.

25

119. **PRO193**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO193. In particular, Applicants have identified and isolated cDNA encoding a PRO193 polypeptide, as disclosed in further detail in the Examples below. The PRO193-encoding
30 clone was isolated from a human retina library.

120. **PRO1130**

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1130 (shown in Figure 240 and SEQ ID NO:415) has amino acid sequence identity with
35 the human 2-19 protein. Accordingly, it is presently believed that PRO1130 disclosed in the present application is a newly identified 2-19 protein homolog.

121. PRO1335

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1335 (shown in Figure 242 and SEQ ID NO:423) has certain amino acid sequence identity with the human carbonic anhydrase precursor protein (AF037335_1). Accordingly, it is presently believed that PRO1335 disclosed in the present application is a newly identified member of the carbonic anhydrase protein family and may possess activity typical of that family.

122. PRO1329

The DNA66660-1585 clone is believed to encode a secreted factor. As far as is known, the DNA66660-1585 sequence encodes a novel factor designated herein as PRO1329; using WU-BLAST2 sequence alignment computer programs, sequence identities to known proteins were revealed but determined not to be significant.

123. PRO1550

The DNA76393-1664 clone was isolated from a subtracted human breast tumor tissue library. As far as is known, the DNA76393-1664 sequence encodes a novel factor designated herein as PRO1550; using WU-BLAST2 sequence alignment computer programs, sequence identities to known proteins were revealed but determined not to be significant.

B. PRO Variants

In addition to the full-length native sequence PRO polypeptides described herein, it is contemplated that PRO variants can be prepared. PRO variants can be prepared by introducing appropriate nucleotide changes into the PRO DNA, and/or by synthesis of the desired PRO polypeptide. Those skilled in the art will appreciate that amino acid changes may alter post-translational processes of the PRO, such as changing the number or position of glycosylation sites or altering the membrane anchoring characteristics.

Variations in the native full-length sequence PRO or in various domains of the PRO described herein, can be made, for example, using any of the techniques and guidelines for conservative and non-conservative mutations set forth, for instance, in U.S. Patent No. 5,364,934. Variations may be a substitution, deletion or insertion of one or more codons encoding the PRO that results in a change in the amino acid sequence of the PRO as compared with the native sequence PRO. Optionally the variation is by substitution of at least one amino acid with any other amino acid in one or more of the domains of the PRO. Guidance in determining which amino acid residue may be inserted, substituted or deleted without adversely affecting the desired activity may be found by comparing the sequence of the PRO with that of homologous known protein molecules and minimizing the number of amino acid sequence changes made in regions of high homology. Amino acid substitutions can be the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, such as the replacement of a leucine with a serine, i.e., conservative amino acid replacements. Insertions or deletions may optionally be in the range of about 1 to 5 amino acids. The variation allowed may be determined by systematically making insertions, deletions or substitutions of amino acids in the sequence and testing the resulting variants for activity exhibited by the full-length or mature native sequence.

PRO polypeptide fragments are provided herein. Such fragments may be truncated at the N-terminus or C-terminus, or may lack internal residues, for example, when compared with a full length native protein. Certain fragments lack amino acid residues that are not essential for a desired biological activity of the PRO polypeptide.

PRO fragments may be prepared by any of a number of conventional techniques. Desired peptide fragments may be chemically synthesized. An alternative approach involves generating PRO fragments by enzymatic digestion, e.g., by treating the protein with an enzyme known to cleave proteins at sites defined by particular amino acid residues, or by digesting the DNA with suitable restriction enzymes and isolating the desired fragment. Yet another suitable technique involves isolating and amplifying a DNA fragment encoding a desired polypeptide fragment, by polymerase chain reaction (PCR). Oligonucleotides that define the desired termini of the DNA fragment are employed at the 5' and 3' primers in the PCR. Preferably, PRO polypeptide fragments share at least one biological and/or immunological activity with the native PRO polypeptide disclosed herein.

In particular embodiments, conservative substitutions of interest are shown in Table 1 under the heading of preferred substitutions. If such substitutions result in a change in biological activity, then more substantial changes, denominated exemplary substitutions in Table 1, or as further described below in reference to amino acid classes, are introduced and the products screened.

Table 1

	<u>Original Residue</u>	<u>Exemplary Substitutions</u>	<u>Preferred Substitutions</u>
5	Ala (A)	val; leu; ile	val
	Arg (R)	lys; gln; asn	lys
	Asn (N)	gln; his; lys; arg	gln
	Asp (D)	glu	glu
	Cys (C)	ser	ser
10	Gln (Q)	asn	asn
	Glu (E)	asp	asp
	Gly (G)	pro; ala	ala
	His (H)	asn; gln; lys; arg	arg
	Ile (I)	leu; val; met; ala; phe;	
15		norleucine	leu
	Leu (L)	norleucine; ile; val;	
		met; ala; phe	ile
	Lys (K)	arg; gln; asn	arg
	Met (M)	leu; phe; ile	leu
20	Phe (F)	leu; val; ile; ala; tyr	leu
	Pro (P)	ala	ala
	Ser (S)	thr	thr
	Thr (T)	ser	ser
	Trp (W)	tyr; phe	tyr
25	Tyr (Y)	trp; phe; thr; ser	phe
	Val (V)	ile; leu; met; phe;	
		ala; norleucine	leu

Substantial modifications in function or immunological identity of the PRO polypeptide are accomplished by selecting substitutions that differ significantly in their effect on maintaining (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a sheet or helical conformation, (b) the charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain. Naturally occurring residues are divided into groups based on common side-chain properties:

- (1) hydrophobic: norleucine, met, ala, val, leu, ile;
- (2) neutral hydrophilic: cys, ser, thr;
- (3) acidic: asp, glu;
- (4) basic: asn, gln, his, lys, arg;
- (5) residues that influence chain orientation: gly, pro; and
- (6) aromatic: trp, tyr, phe.

Non-conservative substitutions will entail exchanging a member of one of these classes for another class. Such substituted residues also may be introduced into the conservative substitution sites or, more preferably, into the remaining (non-conserved) sites.

The variations can be made using methods known in the art such as oligonucleotide-mediated (site-directed) mutagenesis, alanine scanning, and PCR mutagenesis. Site-directed mutagenesis [Carter et al., Nucl. Acids Res., 13:4331 (1986); Zoller et al., Nucl. Acids Res., 10:6487 (1987)], cassette mutagenesis [Wells et al., Gene, 34:315 (1985)], restriction selection mutagenesis [Wells et al., Philos. Trans. R. Soc. London Ser. A, 317:415 (1986)] or other known techniques can be performed on the cloned DNA to produce the PRO variant

DNA.

Scanning amino acid analysis can also be employed to identify one or more amino acids along a contiguous sequence. Among the preferred scanning amino acids are relatively small, neutral amino acids. Such amino acids include alanine, glycine, serine, and cysteine. Alanine is typically a preferred scanning amino acid among this group because it eliminates the side-chain beyond the beta-carbon and is less likely to alter the main-chain conformation of the variant [Cunningham and Wells, Science, 244: 1081-1085 (1989)]. Alanine is also typically preferred because it is the most common amino acid. Further, it is frequently found in both buried and exposed positions [Creighton, The Proteins, (W.H. Freeman & Co., N.Y.); Chothia, J. Mol. Biol., 150:1 (1976)]. If alanine substitution does not yield adequate amounts of variant, an isoteric amino acid can be used.

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C. Modifications of PRO

Covalent modifications of PRO are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of a PRO polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N- or C- terminal residues of the PRO. Derivatization with bifunctional agents is useful, for instance, for crosslinking PRO to a water-insoluble support matrix or surface for use in the method for purifying anti-PRO antibodies, and vice-versa. Commonly used crosslinking agents include, e.g., 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), bifunctional maleimides such as bis-N-maleimido-1,8-octane and agents such as methyl-3-[(p-azidophenyl)dithio]propioimide.

20

Other modifications include deamidation of glutamyl and asparaginyl residues to the corresponding glutamyl and aspartyl residues, respectively, hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of seryl or threonyl residues, methylation of the α -amino groups of lysine, arginine, and histidine side chains [T.E. Creighton, Proteins: Structure and Molecular Properties, W.H. Freeman & Co., San Francisco, pp. 79-86 (1983)], acetylation of the N-terminal amine, and amidation of any C-terminal carboxyl group.

25

Another type of covalent modification of the PRO polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of the polypeptide. "Altering the native glycosylation pattern" is intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence PRO (either by removing the underlying glycosylation site or by deleting the glycosylation by chemical and/or enzymatic means), and/or adding one or more glycosylation sites that are not present in the native sequence PRO. In addition, the phrase includes qualitative changes in the glycosylation of the native proteins, involving a change in the nature and proportions of the various carbohydrate moieties present.

30

Addition of glycosylation sites to the PRO polypeptide may be accomplished by altering the amino acid sequence. The alteration may be made, for example, by the addition of, or substitution by, one or more serine or threonine residues to the native sequence PRO (for O-linked glycosylation sites). The PRO amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the PRO polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

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Another means of increasing the number of carbohydrate moieties on the PRO polypeptide is by chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., in WO 87/05330 published 11 September 1987, and in Aplin and Wriston, CRC Crit. Rev. Biochem., pp. 259-306 (1981).

Removal of carbohydrate moieties present on the PRO polypeptide may be accomplished chemically or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets for glycosylation. Chemical deglycosylation techniques are known in the art and described, for instance, by Hakimuddin, et al., Arch. Biochem. Biophys., 259:52 (1987) and by Edge et al., Anal. Biochem., 118:131 (1981). Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a variety of endo- and exo-glycosidases as described by Thotakura et al., Meth. Enzymol., 138:350 (1987).

Another type of covalent modification of PRO comprises linking the PRO polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol (PEG), polypropylene glycol, or polyoxyalkylenes, in the manner set forth in U.S. Patent Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192 or 4,179,337.

The PRO of the present invention may also be modified in a way to form a chimeric molecule comprising PRO fused to another, heterologous polypeptide or amino acid sequence.

In one embodiment, such a chimeric molecule comprises a fusion of the PRO with a tag polypeptide which provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is generally placed at the amino- or carboxyl- terminus of the PRO. The presence of such epitope-tagged forms of the PRO can be detected using an antibody against the tag polypeptide. Also, provision of the epitope tag enables the PRO to be readily purified by affinity purification using an anti-tag antibody or another type of affinity matrix that binds to the epitope tag. Various tag polypeptides and their respective antibodies are well known in the art. Examples include poly-histidine (poly-his) or poly-histidine-glycine (poly-his-gly) tags; the flu HA tag polypeptide and its antibody 12CA5 [Field et al., Mol. Cell. Biol., 8:2159-2165 (1988)]; the c-myc tag and the 8F9, 3C7, 6E10, G4, B7 and 9E10 antibodies thereto [Evan et al., Molecular and Cellular Biology, 5:3610-3616 (1985)]; and the Herpes Simplex virus glycoprotein D (gD) tag and its antibody [Paborsky et al., Protein Engineering, 3(6):547-553 (1990)]. Other tag polypeptides include the Flag-peptide [Hopp et al., BioTechnology, 6:1204-1210 (1988)]; the KT3 epitope peptide [Martin et al., Science, 255:192-194 (1992)]; an α -tubulin epitope peptide [Skinner et al., J. Biol. Chem., 266:15163-15166 (1991)]; and the T7 gene 10 protein peptide tag [Lutz-Freyermuth et al., Proc. Natl. Acad. Sci. USA, 87:6393-6397 (1990)].

In an alternative embodiment, the chimeric molecule may comprise a fusion of the PRO with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule (also referred to as an "immunoadhesin"), such a fusion could be to the Fc region of an IgG molecule. The Ig fusions preferably include the substitution of a soluble (transmembrane domain deleted or inactivated) form of a PRO polypeptide in place of at least one variable region within an Ig molecule. In a particularly preferred embodiment, the immunoglobulin fusion includes the hinge, CH2 and CH3, or the hinge, CH1, CH2 and CH3 regions of an IgG1 molecule. For the production of immunoglobulin fusions see also US Patent No. 5,428,130 issued June 27, 1995.

D. Preparation of PRO

The description below relates primarily to production of PRO by culturing cells transformed or transfected with a vector containing PRO nucleic acid. It is, of course, contemplated that alternative methods, which are well known in the art, may be employed to prepare PRO. For instance, the PRO sequence, or portions thereof, may be produced by direct peptide synthesis using solid-phase techniques [see, e.g., Stewart et al., Solid-Phase Peptide Synthesis, W.H. Freeman Co., San Francisco, CA (1969); Merrifield, J. Am. Chem. Soc., 85:2149-2154 (1963)]. *In vitro* protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be accomplished, for instance, using an Applied Biosystems Peptide Synthesizer (Foster City, CA) using manufacturer's instructions. Various portions of the PRO may be chemically synthesized separately and combined using chemical or enzymatic methods to produce the full-length PRO.

1. Isolation of DNA Encoding PRO

DNA encoding PRO may be obtained from a cDNA library prepared from tissue believed to possess the PRO mRNA and to express it at a detectable level. Accordingly, human PRO DNA can be conveniently obtained from a cDNA library prepared from human tissue, such as described in the Examples. The PRO-encoding gene may also be obtained from a genomic library or by known synthetic procedures (e.g., automated nucleic acid synthesis).

Libraries can be screened with probes (such as antibodies to the PRO or oligonucleotides of at least about 20-80 bases) designed to identify the gene of interest or the protein encoded by it. Screening the cDNA or genomic library with the selected probe may be conducted using standard procedures, such as described in Sambrook et al., Molecular Cloning: A Laboratory Manual (New York: Cold Spring Harbor Laboratory Press, 1989). An alternative means to isolate the gene encoding PRO is to use PCR methodology [Sambrook et al., supra; Dieffenbach et al., PCR Primer: A Laboratory Manual (Cold Spring Harbor Laboratory Press, 1995)].

The Examples below describe techniques for screening a cDNA library. The oligonucleotide sequences selected as probes should be of sufficient length and sufficiently unambiguous that false positives are minimized. The oligonucleotide is preferably labeled such that it can be detected upon hybridization to DNA in the library being screened. Methods of labeling are well known in the art, and include the use of radiolabels like ³²P-labeled ATP, biotinylation or enzyme labeling. Hybridization conditions, including moderate stringency and high stringency, are provided in Sambrook et al., supra.

Sequences identified in such library screening methods can be compared and aligned to other known sequences deposited and available in public databases such as GenBank or other private sequence databases. Sequence identity (at either the amino acid or nucleotide level) within defined regions of the molecule or across the full-length sequence can be determined using methods known in the art and as described herein.

Nucleic acid having protein coding sequence may be obtained by screening selected cDNA or genomic libraries using the deduced amino acid sequence disclosed herein for the first time, and, if necessary, using conventional primer extension procedures as described in Sambrook et al., supra, to detect precursors and processing intermediates of mRNA that may not have been reverse-transcribed into cDNA.

2. Selection and Transformation of Host Cells

Host cells are transfected or transformed with expression or cloning vectors described herein for PRO production and cultured in conventional nutrient media modified as appropriate for inducing promoters, selecting transformants, or amplifying the genes encoding the desired sequences. The culture conditions, such as media, temperature, pH and the like, can be selected by the skilled artisan without undue experimentation. In general, principles, protocols, and practical techniques for maximizing the productivity of cell cultures can be found in Mammalian Cell Biotechnology: a Practical Approach, M. Butler, ed. (IRL Press, 1991) and Sambrook et al., supra.

Methods of eukaryotic cell transfection and prokaryotic cell transformation are known to the ordinarily skilled artisan, for example, CaCl_2 , CaPO_4 , liposome-mediated and electroporation. Depending on the host cell used, transformation is performed using standard techniques appropriate to such cells. The calcium treatment employing calcium chloride, as described in Sambrook et al., supra, or electroporation is generally used for prokaryotes. Infection with *Agrobacterium tumefaciens* is used for transformation of certain plant cells, as described by Shaw et al., Gene, 23:315 (1983) and WO 89/05859 published 29 June 1989. For mammalian cells without such cell walls, the calcium phosphate precipitation method of Graham and van der Eb, Virology, 52:456-457 (1978) can be employed. General aspects of mammalian cell host system transfections have been described in U.S. Patent No. 4,399,216. Transformations into yeast are typically carried out according to the method of Van Solingen et al., J. Bact., 130:946 (1977) and Hsiao et al., Proc. Natl. Acad. Sci. (USA), 76:3829 (1979). However, other methods for introducing DNA into cells, such as by nuclear microinjection, electroporation, bacterial protoplast fusion with intact cells, or polycations, e.g., polybrene, polyornithine, may also be used. For various techniques for transforming mammalian cells, see Keown et al., Methods in Enzymology, 185:527-537 (1990) and Mansour et al., Nature, 336:348-352 (1988).

Suitable host cells for cloning or expressing the DNA in the vectors herein include prokaryote, yeast, or higher eukaryote cells. Suitable prokaryotes include but are not limited to eubacteria, such as Gram-negative or Gram-positive organisms, for example, Enterobacteriaceae such as *E. coli*. Various *E. coli* strains are publicly available, such as *E. coli* K12 strain MM294 (ATCC 31,446); *E. coli* X1776 (ATCC 31,537); *E. coli* strain W3110 (ATCC 27,325) and K5 772 (ATCC 53,635). Other suitable prokaryotic host cells include Enterobacteriaceae such as *Escherichia*, e.g., *E. coli*, *Enterobacter*, *Erwinia*, *Klebsiella*, *Proteus*, *Salmonella*, e.g., *Salmonella typhimurium*, *Serratia*, e.g., *Serratia marcescans*, and *Shigella*, as well as *Bacilli* such as *B. subtilis* and *B. licheniformis* (e.g., *B. licheniformis* 41P disclosed in DD 266,710 published 12 April 1989), *Pseudomonas* such as *P. aeruginosa*, and *Streptomyces*. These examples are illustrative rather than limiting. Strain W3110 is one particularly preferred host or parent host because it is a common host strain for recombinant DNA product fermentations. Preferably, the host cell secretes minimal amounts of proteolytic enzymes. For example, strain W3110 may be modified to effect a genetic mutation in the genes encoding proteins endogenous to the host, with examples of such hosts including *E. coli* W3110 strain 1A2, which has the complete genotype *tonA*; *E. coli* W3110 strain 9E4, which has the complete genotype *tonA ptr3*; *E. coli* W3110 strain 27C7 (ATCC 55,244), which has the complete genotype *tonA ptr3 phoA E15 (argF-lac)169 degP ompT kan'*; *E. coli* W3110 strain 37D6, which has the complete genotype *tonA ptr3 phoA E15 (argF-lac)169 degP ompT rbs7*

ilvG kan^r; *E. coli* W3110 strain 40B4, which is strain 37D6 with a non-kanamycin resistant *degP* deletion mutation; and an *E. coli* strain having mutant periplasmic protease disclosed in U.S. Patent No. 4,946,783 issued 7 August 1990. Alternatively, *in vitro* methods of cloning, e.g., PCR or other nucleic acid polymerase reactions, are suitable.

In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeast are suitable cloning or expression hosts for PRO-encoding vectors. *Saccharomyces cerevisiae* is a commonly used lower eukaryotic host microorganism. Others include *Schizosaccharomyces pombe* (Beach and Nurse, Nature, 290: 140 [1981]; EP 139,383 published 2 May 1985); *Kluyveromyces* hosts (U.S. Patent No. 4,943,529; Fleer et al., Bio/Technology, 9:968-975 (1991)) such as, e.g., *K. lactis* (MW98-8C, CBS683, CBS4574; Louvencourt et al., J. Bacteriol., 737 [1983]), *K. fragilis* (ATCC 12,424), *K. bulgaricus* (ATCC 16,045), *K. wickerhamii* (ATCC 24,178), *K. waltii* (ATCC 56,500), *K. drosophilae* (ATCC 36,906; Van den Berg et al., Bio/Technology, 8:135 (1990)), *K. thermotolerans*, and *K. marxianus*; *yarrowia* (EP 402,226); *Pichia pastoris* (EP 183,070; Sreekrishna et al., J. Basic Microbiol., 28:265-278 [1988]); *Candida*; *Trichoderma reesia* (EP 244,234); *Neurospora crassa* (Case et al., Proc. Natl. Acad. Sci. USA, 76:5259-5263 [1979]); *Schwanniomyces* such as *Schwanniomyces occidentalis* (EP 394,538 published 31 October 1990); and filamentous fungi such as, e.g., *Neurospora*, *Penicillium*, *Tolypocladium* (WO 91/00357 published 10 January 1991), and *Aspergillus* hosts such as *A. nidulans* (Ballance et al., Biochem. Biophys. Res. Commun., 112:284-289 [1983]; Tilburn et al., Gene, 26:205-221 [1983]; Yelton et al., Proc. Natl. Acad. Sci. USA, 81: 1470-1474 [1984]) and *A. niger* (Kelly and Hynes, EMBO J., 4:475-479 [1985]). Methylophilic yeasts are suitable herein and include, but are not limited to, yeast capable of growth on methanol selected from the genera consisting of *Hansenula*, *Candida*, *Kloeckera*, *Pichia*, *Saccharomyces*, *Torulopsis*, and *Rhodotorula*. A list of specific species that are exemplary of this class of yeasts may be found in C. Anthony, The Biochemistry of Methylophilic Yeasts, 269 (1982).

Suitable host cells for the expression of glycosylated PRO are derived from multicellular organisms. Examples of invertebrate cells include insect cells such as *Drosophila* S2 and *Spodoptera* Sf9, as well as plant cells. Examples of useful mammalian host cell lines include Chinese hamster ovary (CHO) and COS cells. More specific examples include monkey kidney CV1 line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham et al., J. Gen Virol., 36:59 (1977)); Chinese hamster ovary cells/-DHFR (CHO, Urlaub and Chasin, Proc. Natl. Acad. Sci. USA, 77:4216 (1980)); mouse sertoli cells (TM4, Mather, Biol. Reprod., 23:243-251 (1980)); human lung cells (W138, ATCC CCL 75); human liver cells (Hep G2, HB 8065); and mouse mammary tumor (MMT 060562, ATCC CCL51). The selection of the appropriate host cell is deemed to be within the skill in the art.

3. Selection and Use of a Replicable Vector

The nucleic acid (e.g., cDNA or genomic DNA) encoding PRO may be inserted into a replicable vector for cloning (amplification of the DNA) or for expression. Various vectors are publicly available. The vector may, for example, be in the form of a plasmid, cosmid, viral particle, or phage. The appropriate nucleic acid sequence may be inserted into the vector by a variety of procedures. In general, DNA is inserted into an appropriate restriction endonuclease site(s) using techniques known in the art. Vector components generally

include, but are not limited to, one or more of a signal sequence, an origin of replication, one or more marker genes, an enhancer element, a promoter, and a transcription termination sequence. Construction of suitable vectors containing one or more of these components employs standard ligation techniques which are known to the skilled artisan.

5 The PRO may be produced recombinantly not only directly, but also as a fusion polypeptide with a heterologous polypeptide, which may be a signal sequence or other polypeptide having a specific cleavage site at the N-terminus of the mature protein or polypeptide. In general, the signal sequence may be a component of the vector, or it may be a part of the PRO-encoding DNA that is inserted into the vector. The signal sequence may be a prokaryotic signal sequence selected, for example, from the group of the alkaline phosphatase, penicillinase, lpp, or heat-stable enterotoxin II leaders. For yeast secretion the signal sequence may be, e.g.,
10 the yeast invertase leader, alpha factor leader (including *Saccharomyces* and *Kluyveromyces* α -factor leaders, the latter described in U.S. Patent No. 5,010,182), or acid phosphatase leader, the *C. albicans* glucoamylase leader (EP 362,179 published 4 April 1990), or the signal described in WO 90/13646 published 15 November 1990. In mammalian cell expression, mammalian signal sequences may be used to direct secretion of the protein, such as signal sequences from secreted polypeptides of the same or related species, as well as viral
15 secretory leaders.

Both expression and cloning vectors contain a nucleic acid sequence that enables the vector to replicate in one or more selected host cells. Such sequences are well known for a variety of bacteria, yeast, and viruses. The origin of replication from the plasmid pBR322 is suitable for most Gram-negative bacteria, the 2 μ plasmid origin is suitable for yeast, and various viral origins (SV40, polyoma, adenovirus, VSV or BPV) are useful for
20 cloning vectors in mammalian cells.

Expression and cloning vectors will typically contain a selection gene, also termed a selectable marker. Typical selection genes encode proteins that (a) confer resistance to antibiotics or other toxins, e.g., ampicillin, neomycin, methotrexate, or tetracycline, (b) complement auxotrophic deficiencies, or (c) supply critical nutrients not available from complex media, e.g., the gene encoding D-alanine racemase for *Bacilli*.

25 An example of suitable selectable markers for mammalian cells are those that enable the identification of cells competent to take up the PRO-encoding nucleic acid, such as DHFR or thymidine kinase. An appropriate host cell when wild-type DHFR is employed is the CHO cell line deficient in DHFR activity, prepared and propagated as described by Urlaub et al., Proc. Natl. Acad. Sci. USA, 77:4216 (1980). A suitable selection gene for use in yeast is the *trp1* gene present in the yeast plasmid YRp7 [Stinchcomb et al., Nature,
30 282:39 (1979); Kingsman et al., Gene, 7:141 (1979); Tschemper et al., Gene, 10:157 (1980)]. The *trp1* gene provides a selection marker for a mutant strain of yeast lacking the ability to grow in tryptophan, for example, ATCC No. 44076 or PEP4-1 [Jones, Genetics, 85:12 (1977)].

Expression and cloning vectors usually contain a promoter operably linked to the PRO-encoding nucleic acid sequence to direct mRNA synthesis. Promoters recognized by a variety of potential host cells are well
35 known. Promoters suitable for use with prokaryotic hosts include the β -lactamase and lactose promoter systems [Chang et al., Nature, 275:615 (1978); Goeddel et al., Nature, 281:544 (1979)], alkaline phosphatase, a tryptophan (*trp*) promoter system [Goeddel, Nucleic Acids Res., 8:4057 (1980); EP 36,776], and hybrid

promoters such as the tac promoter [deBoer et al., Proc. Natl. Acad. Sci. USA, 80:21-25 (1983)]. Promoters for use in bacterial systems also will contain a Shine-Dalgarno (S.D.) sequence operably linked to the DNA encoding PRO.

5 Examples of suitable promoting sequences for use with yeast hosts include the promoters for 3-phosphoglycerate kinase [Hitzeman et al., J. Biol. Chem., 255:2073 (1980)] or other glycolytic enzymes [Hess et al., J. Adv. Enzyme Reg., 7:149 (1968); Holland, Biochemistry, 17:4900 (1978)], such as enolase, glyceraldehyde-3-phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase, and glucokinase.

10 Other yeast promoters, which are inducible promoters having the additional advantage of transcription controlled by growth conditions, are the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, degradative enzymes associated with nitrogen metabolism, metallothionein, glyceraldehyde-3-phosphate dehydrogenase, and enzymes responsible for maltose and galactose utilization. Suitable vectors and promoters for use in yeast expression are further described in EP 73,657.

15 PRO transcription from vectors in mammalian host cells is controlled, for example, by promoters obtained from the genomes of viruses such as polyoma virus, fowlpox virus (UK 2,211,504 published 5 July 1989), adenovirus (such as Adenovirus 2), bovine papilloma virus, avian sarcoma virus, cytomegalovirus, a retrovirus, hepatitis-B virus and Simian Virus 40 (SV40), from heterologous mammalian promoters, e.g., the actin promoter or an immunoglobulin promoter, and from heat-shock promoters, provided such promoters are compatible with the host cell systems.

20 Transcription of a DNA encoding the PRO by higher eukaryotes may be increased by inserting an enhancer sequence into the vector. Enhancers are cis-acting elements of DNA, usually about from 10 to 300 bp, that act on a promoter to increase its transcription. Many enhancer sequences are now known from mammalian genes (globin, elastase, albumin, α -fetoprotein, and insulin). Typically, however, one will use an enhancer from a eukaryotic cell virus. Examples include the SV40 enhancer on the late side of the replication
25 origin (bp 100-270), the cytomegalovirus early promoter enhancer, the polyoma enhancer on the late side of the replication origin, and adenovirus enhancers. The enhancer may be spliced into the vector at a position 5' or 3' to the PRO coding sequence, but is preferably located at a site 5' from the promoter.

30 Expression vectors used in eukaryotic host cells (yeast, fungi, insect, plant, animal, human, or nucleated cells from other multicellular organisms) will also contain sequences necessary for the termination of transcription and for stabilizing the mRNA. Such sequences are commonly available from the 5' and, occasionally 3', untranslated regions of eukaryotic or viral DNAs or cDNAs. These regions contain nucleotide segments transcribed as polyadenylated fragments in the untranslated portion of the mRNA encoding PRO.

Still other methods, vectors, and host cells suitable for adaptation to the synthesis of PRO in recombinant vertebrate cell culture are described in Gething et al., Nature, 293:620-625 (1981); Mantei et al.,
35 Nature, 281:40-46 (1979); EP 117,060; and EP 117,058.

4. Detecting Gene Amplification/Expression

Gene amplification and/or expression may be measured in a sample directly, for example, by conventional Southern blotting, Northern blotting to quantitate the transcription of mRNA [Thomas, Proc. Natl. Acad. Sci. USA, 77:5201-5205 (1980)], dot blotting (DNA analysis), or *in situ* hybridization, using an appropriately labeled probe, based on the sequences provided herein. Alternatively, antibodies may be employed that can recognize specific duplexes, including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes or DNA-protein duplexes. The antibodies in turn may be labeled and the assay may be carried out where the duplex is bound to a surface, so that upon the formation of duplex on the surface, the presence of antibody bound to the duplex can be detected.

Gene expression, alternatively, may be measured by immunological methods, such as immunohistochemical staining of cells or tissue sections and assay of cell culture or body fluids, to quantitate directly the expression of gene product. Antibodies useful for immunohistochemical staining and/or assay of sample fluids may be either monoclonal or polyclonal, and may be prepared in any mammal. Conveniently, the antibodies may be prepared against a native sequence PRO polypeptide or against a synthetic peptide based on the DNA sequences provided herein or against exogenous sequence fused to PRO DNA and encoding a specific antibody epitope.

5. Purification of Polypeptide

Forms of PRO may be recovered from culture medium or from host cell lysates. If membrane-bound, it can be released from the membrane using a suitable detergent solution (e.g. Triton-X 100) or by enzymatic cleavage. Cells employed in expression of PRO can be disrupted by various physical or chemical means, such as freeze-thaw cycling, sonication, mechanical disruption, or cell lysing agents.

It may be desired to purify PRO from recombinant cell proteins or polypeptides. The following procedures are exemplary of suitable purification procedures: by fractionation on an ion-exchange column; ethanol precipitation; reverse phase HPLC; chromatography on silica or on a cation-exchange resin such as DEAE; chromatofocusing; SDS-PAGE; ammonium sulfate precipitation; gel filtration using, for example, Sephadex G-75; protein A Sepharose columns to remove contaminants such as IgG; and metal chelating columns to bind epitope-tagged forms of the PRO. Various methods of protein purification may be employed and such methods are known in the art and described for example in Deutscher, Methods in Enzymology, 182 (1990); Scopes, Protein Purification: Principles and Practice, Springer-Verlag, New York (1982). The purification step(s) selected will depend, for example, on the nature of the production process used and the particular PRO produced.

E. Uses for PRO

Nucleotide sequences (or their complement) encoding PRO have various applications in the art of molecular biology, including uses as hybridization probes, in chromosome and gene mapping and in the generation of anti-sense RNA and DNA. PRO nucleic acid will also be useful for the preparation of PRO polypeptides by the recombinant techniques described herein.

The full-length native sequence PRO gene, or portions thereof, may be used as hybridization probes for a cDNA library to isolate the full-length PRO cDNA or to isolate still other cDNAs (for instance, those encoding naturally-occurring variants of PRO or PRO from other species) which have a desired sequence identity to the native PRO sequence disclosed herein. Optionally, the length of the probes will be about 20 to about 50 bases. The hybridization probes may be derived from at least partially novel regions of the full length native nucleotide sequence wherein those regions may be determined without undue experimentation or from genomic sequences including promoters, enhancer elements and introns of native sequence PRO. By way of example, a screening method will comprise isolating the coding region of the PRO gene using the known DNA sequence to synthesize a selected probe of about 40 bases. Hybridization probes may be labeled by a variety of labels, including radionucleotides such as ^{32}P or ^{35}S , or enzymatic labels such as alkaline phosphatase coupled to the probe via avidin/biotin coupling systems. Labeled probes having a sequence complementary to that of the PRO gene of the present invention can be used to screen libraries of human cDNA, genomic DNA or mRNA to determine which members of such libraries the probe hybridizes to. Hybridization techniques are described in further detail in the Examples below.

Any EST sequences disclosed in the present application may similarly be employed as probes, using the methods disclosed herein.

Other useful fragments of the PRO nucleic acids include antisense or sense oligonucleotides comprising a single-stranded nucleic acid sequence (either RNA or DNA) capable of binding to target PRO mRNA (sense) or PRO DNA (antisense) sequences. Antisense or sense oligonucleotides, according to the present invention, comprise a fragment of the coding region of PRO DNA. Such a fragment generally comprises at least about 14 nucleotides, preferably from about 14 to 30 nucleotides. The ability to derive an antisense or a sense oligonucleotide, based upon a cDNA sequence encoding a given protein is described in, for example, Stein and Cohen (Cancer Res. 48:2659, 1988) and van der Krol et al. (BioTechniques 6:958, 1988).

Binding of antisense or sense oligonucleotides to target nucleic acid sequences results in the formation of duplexes that block transcription or translation of the target sequence by one of several means, including enhanced degradation of the duplexes, premature termination of transcription or translation, or by other means. The antisense oligonucleotides thus may be used to block expression of PRO proteins. Antisense or sense oligonucleotides further comprise oligonucleotides having modified sugar-phosphodiester backbones (or other sugar linkages, such as those described in WO 91/06629) and wherein such sugar linkages are resistant to endogenous nucleases. Such oligonucleotides with resistant sugar linkages are stable *in vivo* (i.e., capable of resisting enzymatic degradation) but retain sequence specificity to be able to bind to target nucleotide sequences.

Other examples of sense or antisense oligonucleotides include those oligonucleotides which are covalently linked to organic moieties, such as those described in WO 90/10048, and other moieties that increases affinity of the oligonucleotide for a target nucleic acid sequence, such as poly-(L-lysine). Further still, intercalating agents, such as ellipticine, and alkylating agents or metal complexes may be attached to sense or antisense oligonucleotides to modify binding specificities of the antisense or sense oligonucleotide for the target nucleotide sequence.

Antisense or sense oligonucleotides may be introduced into a cell containing the target nucleic acid

sequence by any gene transfer method, including, for example, CaPO_4 -mediated DNA transfection, electroporation, or by using gene transfer vectors such as Epstein-Barr virus. In a preferred procedure, an antisense or sense oligonucleotide is inserted into a suitable retroviral vector. A cell containing the target nucleic acid sequence is contacted with the recombinant retroviral vector, either *in vivo* or *ex vivo*. Suitable retroviral vectors include, but are not limited to, those derived from the murine retrovirus M-MuLV, N2 (a retrovirus derived from M-MuLV), or the double copy vectors designated DCT5A, DCT5B and DCT5C (see WO 90/13641).

Sense or antisense oligonucleotides also may be introduced into a cell containing the target nucleotide sequence by formation of a conjugate with a ligand binding molecule, as described in WO 91/04753. Suitable ligand binding molecules include, but are not limited to, cell surface receptors, growth factors, other cytokines, or other ligands that bind to cell surface receptors. Preferably, conjugation of the ligand binding molecule does not substantially interfere with the ability of the ligand binding molecule to bind to its corresponding molecule or receptor, or block entry of the sense or antisense oligonucleotide or its conjugated version into the cell.

Alternatively, a sense or an antisense oligonucleotide may be introduced into a cell containing the target nucleic acid sequence by formation of an oligonucleotide-lipid complex, as described in WO 90/10448. The sense or antisense oligonucleotide-lipid complex is preferably dissociated within the cell by an endogenous lipase.

The probes may also be employed in PCR techniques to generate a pool of sequences for identification of closely related PRO coding sequences.

Nucleotide sequences encoding a PRO can also be used to construct hybridization probes for mapping the gene which encodes that PRO and for the genetic analysis of individuals with genetic disorders. The nucleotide sequences provided herein may be mapped to a chromosome and specific regions of a chromosome using known techniques, such as *in situ* hybridization, linkage analysis against known chromosomal markers, and hybridization screening with libraries.

When the coding sequences for PRO encode a protein which binds to another protein (example, where the PRO is a receptor), the PRO can be used in assays to identify the other proteins or molecules involved in the binding interaction. By such methods, inhibitors of the receptor/ligand binding interaction can be identified. Proteins involved in such binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction. Also, the receptor PRO can be used to isolate correlative ligand(s). Screening assays can be designed to find lead compounds that mimic the biological activity of a native PRO or a receptor for PRO. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates. Small molecules contemplated include synthetic organic or inorganic compounds. The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays and cell based assays, which are well characterized in the art.

Nucleic acids which encode PRO or its modified forms can also be used to generate either transgenic animals or "knock out" animals which, in turn, are useful in the development and screening of therapeutically useful reagents. A transgenic animal (e.g., a mouse or rat) is an animal having cells that contain a transgene, which transgene was introduced into the animal or an ancestor of the animal at a prenatal, e.g., an embryonic

stage. A transgene is a DNA which is integrated into the genome of a cell from which a transgenic animal develops. In one embodiment, cDNA encoding PRO can be used to clone genomic DNA encoding PRO in accordance with established techniques and the genomic sequences used to generate transgenic animals that contain cells which express DNA encoding PRO. Methods for generating transgenic animals, particularly animals such as mice or rats, have become conventional in the art and are described, for example, in U.S. Patent
5 Nos. 4,736,866 and 4,870,009. Typically, particular cells would be targeted for PRO transgene incorporation with tissue-specific enhancers. Transgenic animals that include a copy of a transgene encoding PRO introduced into the germ line of the animal at an embryonic stage can be used to examine the effect of increased expression of DNA encoding PRO. Such animals can be used as tester animals for reagents thought to confer protection from, for example, pathological conditions associated with its overexpression. In accordance with this facet of
10 the invention, an animal is treated with the reagent and a reduced incidence of the pathological condition, compared to untreated animals bearing the transgene, would indicate a potential therapeutic intervention for the pathological condition.

Alternatively, non-human homologues of PRO can be used to construct a PRO "knock out" animal which has a defective or altered gene encoding PRO as a result of homologous recombination between the
15 endogenous gene encoding PRO and altered genomic DNA encoding PRO introduced into an embryonic stem cell of the animal. For example, cDNA encoding PRO can be used to clone genomic DNA encoding PRO in accordance with established techniques. A portion of the genomic DNA encoding PRO can be deleted or replaced with another gene, such as a gene encoding a selectable marker which can be used to monitor integration. Typically, several kilobases of unaltered flanking DNA (both at the 5' and 3' ends) are included
20 in the vector [see e.g., Thomas and Capecchi, *Cell*, 51:503 (1987) for a description of homologous recombination vectors]. The vector is introduced into an embryonic stem cell line (e.g., by electroporation) and cells in which the introduced DNA has homologously recombined with the endogenous DNA are selected [see e.g., Li et al., *Cell*, 69:915 (1992)]. The selected cells are then injected into a blastocyst of an animal (e.g., a mouse or rat) to form aggregation chimeras [see e.g., Bradley, in *Teratocarcinomas and Embryonic Stem*
25 *Cells: A Practical Approach*, E. J. Robertson, ed. (IRL, Oxford, 1987), pp. 113-152]. A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term to create a "knock out" animal. Progeny harboring the homologously recombined DNA in their germ cells can be identified by standard techniques and used to breed animals in which all cells of the animal contain the homologously recombined DNA. Knockout animals can be characterized for instance, for their ability to defend
30 against certain pathological conditions and for their development of pathological conditions due to absence of the PRO polypeptide.

Nucleic acid encoding the PRO polypeptides may also be used in gene therapy. In gene therapy applications, genes are introduced into cells in order to achieve *in vivo* synthesis of a therapeutically effective genetic product, for example for replacement of a defective gene. "Gene therapy" includes both conventional
35 gene therapy where a lasting effect is achieved by a single treatment, and the administration of gene therapeutic agents, which involves the one time or repeated administration of a therapeutically effective DNA or mRNA. Antisense RNAs and DNAs can be used as therapeutic agents for blocking the expression of certain genes *in*

vivo. It has already been shown that short antisense oligonucleotides can be imported into cells where they act as inhibitors, despite their low intracellular concentrations caused by their restricted uptake by the cell membrane. (Zamecnik *et al.*, Proc. Natl. Acad. Sci. USA 83:4143-4146 [1986]). The oligonucleotides can be modified to enhance their uptake, e.g. by substituting their negatively charged phosphodiester groups by uncharged groups.

5 There are a variety of techniques available for introducing nucleic acids into viable cells. The techniques vary depending upon whether the nucleic acid is transferred into cultured cells *in vitro*, or *in vivo* in the cells of the intended host. Techniques suitable for the transfer of nucleic acid into mammalian cells *in vitro* include the use of liposomes, electroporation, microinjection, cell fusion, DEAE-dextran, the calcium phosphate precipitation method, etc. The currently preferred *in vivo* gene transfer techniques include transfection with viral
10 (typically retroviral) vectors and viral coat protein-liposome mediated transfection (Dzau *et al.*, Trends in Biotechnology 11, 205-210 [1993]). In some situations it is desirable to provide the nucleic acid source with an agent that targets the target cells, such as an antibody specific for a cell surface membrane protein or the target cell, a ligand for a receptor on the target cell, etc. Where liposomes are employed, proteins which bind to a cell surface membrane protein associated with endocytosis may be used for targeting and/or to facilitate
15 uptake, e.g. capsid proteins or fragments thereof tropic for a particular cell type, antibodies for proteins which undergo internalization in cycling, proteins that target intracellular localization and enhance intracellular half-life. The technique of receptor-mediated endocytosis is described, for example, by Wu *et al.*, J. Biol. Chem. 262, 4429-4432 (1987); and Wagner *et al.*, Proc. Natl. Acad. Sci. USA 87, 3410-3414 (1990). For review of gene marking and gene therapy protocols see Anderson *et al.*, Science 256, 808-813 (1992).

20 The PRO polypeptides described herein may also be employed as molecular weight markers for protein electrophoresis purposes and the isolated nucleic acid sequences may be used for recombinantly expressing those markers.

 The nucleic acid molecules encoding the PRO polypeptides or fragments thereof described herein are useful for chromosome identification. In this regard, there exists an ongoing need to identify new chromosome
25 markers, since relatively few chromosome marking reagents, based upon actual sequence data are presently available. Each PRO nucleic acid molecule of the present invention can be used as a chromosome marker.

 The PRO polypeptides and nucleic acid molecules of the present invention may also be used for tissue typing, wherein the PRO polypeptides of the present invention may be differentially expressed in one tissue as compared to another. PRO nucleic acid molecules will find use for generating probes for PCR, Northern
30 analysis, Southern analysis and Western analysis.

 The PRO polypeptides described herein may also be employed as therapeutic agents. The PRO polypeptides of the present invention can be formulated according to known methods to prepare pharmaceutically useful compositions, whereby the PRO product hereof is combined in admixture with a pharmaceutically acceptable carrier vehicle. Therapeutic formulations are prepared for storage by mixing the active ingredient
35 having the desired degree of purity with optional physiologically acceptable carriers, excipients or stabilizers (Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980)), in the form of lyophilized formulations or aqueous solutions. Acceptable carriers, excipients or stabilizers are nontoxic to recipients at the

dosages and concentrations employed, and include buffers such as phosphate, citrate and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone, amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEENTM, PLURONICSTM or PEG.

The formulations to be used for *in vivo* administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes, prior to or following lyophilization and reconstitution.

Therapeutic compositions herein generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

The route of administration is in accord with known methods, e.g. injection or infusion by intravenous, intraperitoneal, intracerebral, intramuscular, intraocular, intraarterial or intralesional routes, topical administration, or by sustained release systems.

Dosages and desired drug concentrations of pharmaceutical compositions of the present invention may vary depending on the particular use envisioned. The determination of the appropriate dosage or route of administration is well within the skill of an ordinary physician. Animal experiments provide reliable guidance for the determination of effective doses for human therapy. Interspecies scaling of effective doses can be performed following the principles laid down by Mordenti, J. and Chappell, W. "The use of interspecies scaling in toxicokinetics" In *Toxicokinetics and New Drug Development*, Yacobi et al., Eds., Pergamon Press, New York 1989, pp. 42-96.

When *in vivo* administration of a PRO polypeptide or agonist or antagonist thereof is employed, normal dosage amounts may vary from about 10 ng/kg to up to 100 mg/kg of mammal body weight or more per day, preferably about 1 μ g/kg/day to 10 mg/kg/day, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature; see, for example, U.S. Pat. Nos. 4,657,760; 5,206,344; or 5,225,212. It is anticipated that different formulations will be effective for different treatment compounds and different disorders, that administration targeting one organ or tissue, for example, may necessitate delivery in a manner different from that to another organ or tissue.

Where sustained-release administration of a PRO polypeptide is desired in a formulation with release characteristics suitable for the treatment of any disease or disorder requiring administration of the PRO polypeptide, microencapsulation of the PRO polypeptide is contemplated. Microencapsulation of recombinant proteins for sustained release has been successfully performed with human growth hormone (rhGH), interferon- (rhIFN-), interleukin-2, and MN rgp120. Johnson et al., *Nat. Med.*, 2:795-799 (1996); Yasuda, *Biomed. Ther.*, 27:1221-1223 (1993); Hora et al., *Bio/Technology*, 8:755-758 (1990); Cleland, "Design and Production of Single Immunization Vaccines Using Polylactide Polyglycolide Microsphere Systems," in *Vaccine Design: The Subunit and Adjuvant Approach*, Powell and Newman, eds, (Plenum Press: New York, 1995), pp. 439-462; WO 97/03692, WO 96/40072, WO 96/07399; and U.S. Pat. No. 5,654,010.

The sustained-release formulations of these proteins were developed using poly-lactic-coglycolic acid

(PLGA) polymer due to its biocompatibility and wide range of biodegradable properties. The degradation products of PLGA, lactic and glycolic acids, can be cleared quickly within the human body. Moreover, the degradability of this polymer can be adjusted from months to years depending on its molecular weight and composition. Lewis, "Controlled release of bioactive agents from lactide/glycolide polymer," in: M. Chasin and R. Langer (Eds.), Biodegradable Polymers as Drug Delivery Systems (Marcel Dekker: New York, 1990), pp. 1-41.

This invention encompasses methods of screening compounds to identify those that mimic the PRO polypeptide (agonists) or prevent the effect of the PRO polypeptide (antagonists). Screening assays for antagonist drug candidates are designed to identify compounds that bind or complex with the PRO polypeptides encoded by the genes identified herein, or otherwise interfere with the interaction of the encoded polypeptides with other cellular proteins. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates.

The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays, and cell-based assays, which are well characterized in the art.

All assays for antagonists are common in that they call for contacting the drug candidate with a PRO polypeptide encoded by a nucleic acid identified herein under conditions and for a time sufficient to allow these two components to interact.

In binding assays, the interaction is binding and the complex formed can be isolated or detected in the reaction mixture. In a particular embodiment, the PRO polypeptide encoded by the gene identified herein or the drug candidate is immobilized on a solid phase, e.g., on a microtiter plate, by covalent or non-covalent attachments. Non-covalent attachment generally is accomplished by coating the solid surface with a solution of the PRO polypeptide and drying. Alternatively, an immobilized antibody, e.g., a monoclonal antibody, specific for the PRO polypeptide to be immobilized can be used to anchor it to a solid surface. The assay is performed by adding the non-immobilized component, which may be labeled by a detectable label, to the immobilized component, e.g., the coated surface containing the anchored component. When the reaction is complete, the non-reacted components are removed, e.g., by washing, and complexes anchored on the solid surface are detected. When the originally non-immobilized component carries a detectable label, the detection of label immobilized on the surface indicates that complexing occurred. Where the originally non-immobilized component does not carry a label, complexing can be detected, for example, by using a labeled antibody specifically binding the immobilized complex.

If the candidate compound interacts with but does not bind to a particular PRO polypeptide encoded by a gene identified herein, its interaction with that polypeptide can be assayed by methods well known for detecting protein-protein interactions. Such assays include traditional approaches, such as, e.g., cross-linking, co-immunoprecipitation, and co-purification through gradients or chromatographic columns. In addition, protein-protein interactions can be monitored by using a yeast-based genetic system described by Fields and co-workers (Fields and Song, Nature (London), 340:245-246 (1989); Chien et al., Proc. Natl. Acad. Sci. USA, 88:9578-9582 (1991)) as disclosed by Chevray and Nathans, Proc. Natl. Acad. Sci. USA, 89: 5789-5793 (1991). Many transcriptional activators, such as yeast GAL4, consist of two physically discrete modular domains, one acting

as the DNA-binding domain, the other one functioning as the transcription-activation domain. The yeast expression system described in the foregoing publications (generally referred to as the "two-hybrid system") takes advantage of this property, and employs two hybrid proteins, one in which the target protein is fused to the DNA-binding domain of GAL4, and another, in which candidate activating proteins are fused to the activation domain. The expression of a GAL1-*lacZ* reporter gene under control of a GAL4-activated promoter
5 depends on reconstitution of GAL4 activity via protein-protein interaction. Colonies containing interacting polypeptides are detected with a chromogenic substrate for β -galactosidase. A complete kit (MATCHMAKER™) for identifying protein-protein interactions between two specific proteins using the two-hybrid technique is commercially available from Clontech. This system can also be extended to map protein domains involved in specific protein interactions as well as to pinpoint amino acid residues that are crucial for
10 these interactions.

Compounds that interfere with the interaction of a gene encoding a PRO polypeptide identified herein and other intra- or extracellular components can be tested as follows: usually a reaction mixture is prepared containing the product of the gene and the intra- or extracellular component under conditions and for a time allowing for the interaction and binding of the two products. To test the ability of a candidate compound to
15 inhibit binding, the reaction is run in the absence and in the presence of the test compound. In addition, a placebo may be added to a third reaction mixture, to serve as positive control. The binding (complex formation) between the test compound and the intra- or extracellular component present in the mixture is monitored as described hereinabove. The formation of a complex in the control reaction(s) but not in the reaction mixture containing the test compound indicates that the test compound interferes with the interaction of the test compound
20 and its reaction partner.

To assay for antagonists, the PRO polypeptide may be added to a cell along with the compound to be screened for a particular activity and the ability of the compound to inhibit the activity of interest in the presence of the PRO polypeptide indicates that the compound is an antagonist to the PRO polypeptide. Alternatively, antagonists may be detected by combining the PRO polypeptide and a potential antagonist with membrane-bound
25 PRO polypeptide receptors or recombinant receptors under appropriate conditions for a competitive inhibition assay. The PRO polypeptide can be labeled, such as by radioactivity, such that the number of PRO polypeptide molecules bound to the receptor can be used to determine the effectiveness of the potential antagonist. The gene encoding the receptor can be identified by numerous methods known to those of skill in the art, for example, ligand panning and FACS sorting. Coligan et al., Current Protocols in Immun., 1(2): Chapter 5 (1991).
30 Preferably, expression cloning is employed wherein polyadenylated RNA is prepared from a cell responsive to the PRO polypeptide and a cDNA library created from this RNA is divided into pools and used to transfect COS cells or other cells that are not responsive to the PRO polypeptide. Transfected cells that are grown on glass slides are exposed to labeled PRO polypeptide. The PRO polypeptide can be labeled by a variety of means including iodination or inclusion of a recognition site for a site-specific protein kinase. Following fixation and
35 incubation, the slides are subjected to autoradiographic analysis. Positive pools are identified and sub-pools are prepared and re-transfected using an interactive sub-pooling and re-screening process, eventually yielding a single clone that encodes the putative receptor.

As an alternative approach for receptor identification, labeled PRO polypeptide can be photoaffinity-linked with cell membrane or extract preparations that express the receptor molecule. Cross-linked material is resolved by PAGE and exposed to X-ray film. The labeled complex containing the receptor can be excised, resolved into peptide fragments, and subjected to protein micro-sequencing. The amino acid sequence obtained from micro-sequencing would be used to design a set of degenerate oligonucleotide probes to screen a cDNA library to identify the gene encoding the putative receptor.

In another assay for antagonists, mammalian cells or a membrane preparation expressing the receptor would be incubated with labeled PRO polypeptide in the presence of the candidate compound. The ability of the compound to enhance or block this interaction could then be measured.

More specific examples of potential antagonists include an oligonucleotide that binds to the fusions of immunoglobulin with PRO polypeptide, and, in particular, antibodies including, without limitation, poly- and monoclonal antibodies and antibody fragments, single-chain antibodies, anti-idiotypic antibodies, and chimeric or humanized versions of such antibodies or fragments, as well as human antibodies and antibody fragments. Alternatively, a potential antagonist may be a closely related protein, for example, a mutated form of the PRO polypeptide that recognizes the receptor but imparts no effect, thereby competitively inhibiting the action of the PRO polypeptide.

Another potential PRO polypeptide antagonist is an antisense RNA or DNA construct prepared using antisense technology, where, e.g., an antisense RNA or DNA molecule acts to block directly the translation of mRNA by hybridizing to targeted mRNA and preventing protein translation. Antisense technology can be used to control gene expression through triple-helix formation or antisense DNA or RNA, both of which methods are based on binding of a polynucleotide to DNA or RNA. For example, the 5' coding portion of the polynucleotide sequence, which encodes the mature PRO polypeptides herein, is used to design an antisense RNA oligonucleotide of from about 10 to 40 base pairs in length. A DNA oligonucleotide is designed to be complementary to a region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res., 6:3073 (1979); Cooney et al., Science, 241: 456 (1988); Dervan et al., Science, 251:1360 (1991)), thereby preventing transcription and the production of the PRO polypeptide. The antisense RNA oligonucleotide hybridizes to the mRNA *in vivo* and blocks translation of the mRNA molecule into the PRO polypeptide (antisense - Okano, Neurochem., 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression (CRC Press: Boca Raton, FL, 1988). The oligonucleotides described above can also be delivered to cells such that the antisense RNA or DNA may be expressed *in vivo* to inhibit production of the PRO polypeptide. When antisense DNA is used, oligodeoxyribonucleotides derived from the translation-initiation site, e.g., between about -10 and +10 positions of the target gene nucleotide sequence, are preferred.

Potential antagonists include small molecules that bind to the active site, the receptor binding site, or growth factor or other relevant binding site of the PRO polypeptide, thereby blocking the normal biological activity of the PRO polypeptide. Examples of small molecules include, but are not limited to, small peptides or peptide-like molecules, preferably soluble peptides, and synthetic non-peptidyl organic or inorganic compounds.

Ribozymes are enzymatic RNA molecules capable of catalyzing the specific cleavage of RNA.

Ribozymes act by sequence-specific hybridization to the complementary target RNA, followed by endonucleolytic cleavage. Specific ribozyme cleavage sites within a potential RNA target can be identified by known techniques. For further details see, e.g., Rossi, Current Biology, 4:469-471 (1994), and PCT publication No. WO 97/33551 (published September 18, 1997).

5 Nucleic acid molecules in triple-helix formation used to inhibit transcription should be single-stranded and composed of deoxynucleotides. The base composition of these oligonucleotides is designed such that it promotes triple-helix formation via Hoogsteen base-pairing rules, which generally require sizeable stretches of purines or pyrimidines on one strand of a duplex. For further details see, e.g., PCT publication No. WO 97/33551, *supra*.

10 These small molecules can be identified by any one or more of the screening assays discussed hereinabove and/or by any other screening techniques well known for those skilled in the art.

F. Anti-PRO Antibodies

The present invention further provides anti-PRO antibodies. Exemplary antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies.

15

1. Polyclonal Antibodies

The anti-PRO antibodies may comprise polyclonal antibodies. Methods of preparing polyclonal antibodies are known to the skilled artisan. Polyclonal antibodies can be raised in a mammal, for example, by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent may include the PRO polypeptide or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate). The immunization protocol may be selected by one skilled in the art without undue experimentation.

20

25

2. Monoclonal Antibodies

The anti-PRO antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein, Nature, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized *in vitro*.

30

The immunizing agent will typically include the PRO polypeptide or a fusion protein thereof. Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a

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hybridoma cell [Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103]. Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine

5 guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More

10 preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies [Kozbor, J. Immunol., 133:3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications, Marcel Dekker, Inc., New York, (1987) pp. 51-63].

15 The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against PRO. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an *in vitro* binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the

20 Scatchard analysis of Munson and Pollard, Anal. Biochem., 107:220 (1980).

After the desired hybridoma cells are identified, the clones may be subcloned by limiting dilution procedures and grown by standard methods [Goding, supra]. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells may be grown *in vivo* as ascites in a mammal.

25 The monoclonal antibodies secreted by the subclones may be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

The monoclonal antibodies may also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated

30 and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA may be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal

35 antibodies in the recombinant host cells. The DNA also may be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences [U.S. Patent No. 4,816,567; Morrison et al., supra] or by covalently joining to the immunoglobulin coding

sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

5 The antibodies may be monovalent antibodies. Methods for preparing monovalent antibodies are well known in the art. For example, one method involves recombinant expression of immunoglobulin light chain and modified heavy chain. The heavy chain is truncated generally at any point in the Fc region so as to prevent heavy chain crosslinking. Alternatively, the relevant cysteine residues are substituted with another amino acid residue or are deleted so as to prevent crosslinking.

10 *In vitro* methods are also suitable for preparing monovalent antibodies. Digestion of antibodies to produce fragments thereof, particularly, Fab fragments, can be accomplished using routine techniques known in the art.

3. Human and Humanized Antibodies

15 The anti-PRO antibodies of the invention may further comprise humanized antibodies or human antibodies. Humanized forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')₂ or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues from a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In 20 some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are 25 those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin [Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-329 (1988); and Presta, Curr. Op. Struct. Biol., 2:593-596 (1992)].

30 Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acid residues introduced into it from a source which is non-human. These non-human amino acid residues are often referred to as "import" residues, which are typically taken from an "import" variable domain. Humanization can be essentially performed following the method of Winter and co-workers [Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-327 (1988); Verhoeven et al., 35 Science, 239:1534-1536 (1988)], by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such "humanized" antibodies are chimeric antibodies (U.S. Patent No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the

corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

Human antibodies can also be produced using various techniques known in the art, including phage display libraries [Hoogenboom and Winter, *J. Mol. Biol.*, 227:381 (1991); Marks et al., *J. Mol. Biol.*, 222:581 (1991)]. The techniques of Cole et al. and Boerner et al. are also available for the preparation of human monoclonal antibodies (Cole et al., *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, p. 77 (1985) and Boerner et al., *J. Immunol.*, 147(1):86-95 (1991)]. Similarly, human antibodies can be made by introducing of human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks et al., *Bio/Technology* 10, 779-783 (1992); Lonberg et al., *Nature* 368 856-859 (1994); Morrison, *Nature* 368, 812-13 (1994); Fishwild et al., *Nature Biotechnology* 14, 845-51 (1996); Neuberger, *Nature Biotechnology* 14, 826 (1996); Lonberg and Huszar, *Intern. Rev. Immunol.* 13 65-93 (1995).

4. Bispecific Antibodies

Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for the PRO, the other one is for any other antigen, and preferably for a cell-surface protein or receptor or receptor subunit.

Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities [Milstein and Cuello, *Nature*, 305:537-539 (1983)]. Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Traunecker et al., *EMBO J.*, 10:3655-3659 (1991).

Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light-chain binding present in at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host organism. For further details of generating bispecific antibodies see, for example, Suresh et al., *Methods in Enzymology*, 121:210 (1986).

According to another approach described in WO 96/27011, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (e.g. tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (e.g. alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g. F(ab')₂ bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan *et al.*, Science 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate F(ab')₂ fragments. These fragments are reduced in the presence of the dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Fab' fragments may be directly recovered from *E. coli* and chemically coupled to form bispecific antibodies. Shalaby *et al.*, J. Exp. Med. 175:217-225 (1992) describe the production of a fully humanized bispecific antibody F(ab')₂ molecule. Each Fab' fragment was separately secreted from *E. coli* and subjected to directed chemical coupling *in vitro* to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

Various technique for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny *et al.*, J. Immunol. 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger *et al.*, Proc. Natl. Acad. Sci. USA 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber *et al.*, J. Immunol. 152:5368 (1994).

Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared.

Tutt *et al.*, J. Immunol. 147:60 (1991).

Exemplary bispecific antibodies may bind to two different epitopes on a given PRO polypeptide herein. Alternatively, an anti-PRO polypeptide arm may be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (e.g. CD2, CD3, CD28, or B7), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular PRO polypeptide. Bispecific antibodies may also be used to localize cytotoxic agents to cells which express a particular PRO polypeptide. These antibodies possess a PRO-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the PRO polypeptide and further binds tissue factor (TF).

5. Heteroconjugate Antibodies

Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells [U.S. Patent No. 4,676,980], and for treatment of HIV infection [WO 91/00360; WO 92/200373; EP 03089]. It is contemplated that the antibodies may be prepared *in vitro* using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins may be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

6. Effector Function Engineering

It may be desirable to modify the antibody of the invention with respect to effector function, so as to enhance, *e.g.*, the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) may be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated may have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron *et al.*, J. Exp Med., 176: 1191-1195 (1992) and Shopes, J. Immunol., 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity may also be prepared using heterobifunctional cross-linkers as described in Wolff *et al.* Cancer Research, 53: 2560-2565 (1993). Alternatively, an antibody can be engineered that has dual Fc regions and may thereby have enhanced complement lysis and ADCC capabilities. See Stevenson *et al.*, Anti-Cancer Drug Design, 3: 219-230 (1989).

7. Immunoconjugates

The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (*e.g.*, an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (*i.e.*, a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above.

Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, *Aleurites fordii* proteins, dianthin proteins, *Phytolaca americana* proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radionuclides are
5 available for the production of radioconjugated antibodies. Examples include ^{212}Bi , ^{131}I , ^{131}In , ^{90}Y , and ^{186}Re .

Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutaraldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-
10 diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta *et al.*, Science, 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026.

15 In another embodiment, the antibody may be conjugated to a "receptor" (such streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (*e.g.*, avidin) that is conjugated to a cytotoxic agent (*e.g.*, a radionucleotide).

20 8. Immunoliposomes

The antibodies disclosed herein may also be formulated as immunoliposomes. Liposomes containing the antibody are prepared by methods known in the art, such as described in Epstein *et al.*, Proc. Natl. Acad. Sci. USA, 82: 3688 (1985); Hwang *et al.*, Proc. Natl. Acad. Sci. USA, 77: 4030 (1980); and U.S. Pat. Nos. 4,485,045 and 4,544,545. Liposomes with enhanced circulation time are disclosed in U.S. Patent No.
25 5,013,556.

Particularly useful liposomes can be generated by the reverse-phase evaporation method with a lipid composition comprising phosphatidylcholine, cholesterol, and PEG-derivatized phosphatidylethanolamine (PEG-PE). Liposomes are extruded through filters of defined pore size to yield liposomes with the desired diameter. Fab' fragments of the antibody of the present invention can be conjugated to the liposomes as described in Martin
30 *et al.*, J. Biol. Chem., 257: 286-288 (1982) via a disulfide-interchange reaction. A chemotherapeutic agent (such as Doxorubicin) is optionally contained within the liposome. See Gabizon *et al.*, J. National Cancer Inst., 81(19): 1484 (1989).

9. Pharmaceutical Compositions of Antibodies

35 Antibodies specifically binding a PRO polypeptide identified herein, as well as other molecules identified by the screening assays disclosed hereinbefore, can be administered for the treatment of various disorders in the form of pharmaceutical compositions.

If the PRO polypeptide is intracellular and whole antibodies are used as inhibitors, internalizing antibodies are preferred. However, lipofections or liposomes can also be used to deliver the antibody, or an antibody fragment, into cells. Where antibody fragments are used, the smallest inhibitory fragment that specifically binds to the binding domain of the target protein is preferred. For example, based upon the variable-region sequences of an antibody, peptide molecules can be designed that retain the ability to bind the target protein sequence. Such peptides can be synthesized chemically and/or produced by recombinant DNA technology. See, *e.g.*, Marasco *et al.*, Proc. Natl. Acad. Sci. USA, 90: 7889-7893 (1993). The formulation herein may also contain more than one active compound as necessary for the particular indication being treated, preferably those with complementary activities that do not adversely affect each other. Alternatively, or in addition, the composition may comprise an agent that enhances its function, such as, for example, a cytotoxic agent, cytokine, chemotherapeutic agent, or growth-inhibitory agent. Such molecules are suitably present in combination in amounts that are effective for the purpose intended.

The active ingredients may also be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and poly-(methylmethacrylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles, and nanocapsules) or in macroemulsions. Such techniques are disclosed in Remington's Pharmaceutical Sciences, *supra*.

The formulations to be used for *in vivo* administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes.

Sustained-release preparations may be prepared. Suitable examples of sustained-release preparations include semipermeable matrices of solid hydrophobic polymers containing the antibody, which matrices are in the form of shaped articles, *e.g.*, films, or microcapsules. Examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate), or poly(vinylalcohol)), polylactides (U.S. Pat. No. 3,773,919), copolymers of L-glutamic acid and γ ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as the LUPRON DEPOTTM (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate), and poly-D-(-)-3-hydroxybutyric acid. While polymers such as ethylene-vinyl acetate and lactic acid-glycolic acid enable release of molecules for over 100 days, certain hydrogels release proteins for shorter time periods. When encapsulated antibodies remain in the body for a long time, they may denature or aggregate as a result of exposure to moisture at 37°C, resulting in a loss of biological activity and possible changes in immunogenicity. Rational strategies can be devised for stabilization depending on the mechanism involved. For example, if the aggregation mechanism is discovered to be intermolecular S-S bond formation through thio-disulfide interchange, stabilization may be achieved by modifying sulfhydryl residues, lyophilizing from acidic solutions, controlling moisture content, using appropriate additives, and developing specific polymer matrix compositions.

35 G. Uses for anti-PRO Antibodies

The anti-PRO antibodies of the invention have various utilities. For example, anti-PRO antibodies may be used in diagnostic assays for PRO, *e.g.*, detecting its expression in specific cells, tissues, or serum. Various

diagnostic assay techniques known in the art may be used, such as competitive binding assays, direct or indirect sandwich assays and immunoprecipitation assays conducted in either heterogeneous or homogeneous phases [Zola, Monoclonal Antibodies: A Manual of Techniques, CRC Press, Inc. (1987) pp. 147-158]. The antibodies used in the diagnostic assays can be labeled with a detectable moiety. The detectable moiety should be capable of producing, either directly or indirectly, a detectable signal. For example, the detectable moiety may be a radioisotope, such as ^3H , ^{14}C , ^{32}P , ^{35}S , or ^{125}I , a fluorescent or chemiluminescent compound, such as fluorescein isothiocyanate, rhodamine, or luciferin, or an enzyme, such as alkaline phosphatase, beta-galactosidase or horseradish peroxidase. Any method known in the art for conjugating the antibody to the detectable moiety may be employed, including those methods described by Hunter et al., Nature, 144:945 (1962); David et al., Biochemistry, 13:1014 (1974); Pain et al., J. Immunol. Meth., 40:219 (1981); and Nygren, J. Histochem. and Cytochem., 30:407 (1982).

Anti-PRO antibodies also are useful for the affinity purification of PRO from recombinant cell culture or natural sources. In this process, the antibodies against PRO are immobilized on a suitable support, such as Sephadex resin or filter paper, using methods well known in the art. The immobilized antibody then is contacted with a sample containing the PRO to be purified, and thereafter the support is washed with a suitable solvent that will remove substantially all the material in the sample except the PRO, which is bound to the immobilized antibody. Finally, the support is washed with another suitable solvent that will release the PRO from the antibody.

The following examples are offered for illustrative purposes only, and are not intended to limit the scope of the present invention in any way.

All patent and literature references cited in the present specification are hereby incorporated by reference in their entirety.

EXAMPLES

Commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. The source of those cells identified in the following examples, and throughout the specification, by ATCC accession numbers is the American Type Culture Collection, Manassas, VA.

EXAMPLE 1: Extracellular Domain Homology Screening to Identify Novel Polypeptides and cDNA Encoding Therefor

The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about 950 known secreted proteins from the Swiss-Prot public database were used to search EST databases. The EST databases included public databases (e.g., Dayhoff, GenBank), and proprietary databases (e.g. LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST-2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons with a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA

sequences with the program "phrap" (Phil Green, University of Washington, Seattle, WA).

Using this extracellular domain homology screen, consensus DNA sequences were assembled relative to the other identified EST sequences using phrap. In addition, the consensus DNA sequences obtained were often (but not always) extended using repeated cycles of BLAST or BLAST-2 and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above.

5 Based upon the consensus sequences obtained as described above, oligonucleotides were then synthesized and used to identify by PCR a cDNA library that contained the sequence of interest and for use as probes to isolate a clone of the full-length coding sequence for a PRO polypeptide. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional
10 oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

15 The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

20

EXAMPLE 2: Isolation of cDNA clones by Amylase Screening

1. Preparation of oligo dT primed cDNA library

mRNA was isolated from a human tissue of interest using reagents and protocols from Invitrogen, San Diego, CA (Fast Track 2). This RNA was used to generate an oligo dT primed cDNA library in the vector
25 pRK5D using reagents and protocols from Life Technologies, Gaithersburg, MD (Super Script Plasmid System). In this procedure, the double stranded cDNA was sized to greater than 1000 bp and the SalI/NotI linkered cDNA was cloned into XhoI/NotI cleaved vector. pRK5D is a cloning vector that has an sp6 transcription initiation site followed by an SfiI restriction enzyme site preceding the XhoI/NotI cDNA cloning sites.

30

2. Preparation of random primed cDNA library

A secondary cDNA library was generated in order to preferentially represent the 5' ends of the primary cDNA clones. Sp6 RNA was generated from the primary library (described above), and this RNA was used to generate a random primed cDNA library in the vector pSST-AMY.0 using reagents and protocols from Life Technologies (Super Script Plasmid System, referenced above). In this procedure the double stranded cDNA
35 was sized to 500-1000 bp, linkered with blunt to NotI adaptors, cleaved with SfiI, and cloned into SfiI/NotI cleaved vector. pSST-AMY.0 is a cloning vector that has a yeast alcohol dehydrogenase promoter preceding the cDNA cloning sites and the mouse amylase sequence (the mature sequence without the secretion signal)

followed by the yeast alcohol dehydrogenase terminator, after the cloning sites. Thus, cDNAs cloned into this vector that are fused in frame with amylase sequence will lead to the secretion of amylase from appropriately transfected yeast colonies.

3. Transformation and Detection

5 DNA from the library described in paragraph 2 above was chilled on ice to which was added electrocompetent DH10B bacteria (Life Technologies, 20 ml). The bacteria and vector mixture was then electroporated as recommended by the manufacturer. Subsequently, SOC media (Life Technologies, 1 ml) was added and the mixture was incubated at 37°C for 30 minutes. The transformants were then plated onto 20 standard 150 mm LB plates containing ampicillin and incubated for 16 hours (37°C). Positive colonies were
10 scraped off the plates and the DNA was isolated from the bacterial pellet using standard protocols, e.g. CsCl-gradient. The purified DNA was then carried on to the yeast protocols below.

The yeast methods were divided into three categories: (1) Transformation of yeast with the plasmid/cDNA combined vector; (2) Detection and isolation of yeast clones secreting amylase; and (3) PCR
15 amplification of the insert directly from the yeast colony and purification of the DNA for sequencing and further analysis.

The yeast strain used was HD56-5A (ATCC-90785). This strain has the following genotype: MAT alpha, ura3-52, leu2-3, leu2-112, his3-11, his3-15, MAL⁺, SUC⁺, GAL⁺. Preferably, yeast mutants can be employed that have deficient post-translational pathways. Such mutants may have translocation deficient alleles in *sec71*, *sec72*, *sec62*, with truncated *sec71* being most preferred. Alternatively, antagonists (including
20 antisense nucleotides and/or ligands) which interfere with the normal operation of these genes, other proteins implicated in this post translation pathway (e.g., SEC61p, SEC72p, SEC62p, SEC63p, TDJ1p or SSA1p-4p) or the complex formation of these proteins may also be preferably employed in combination with the amylase-expressing yeast.

Transformation was performed based on the protocol outlined by Gietz et al., Nucl. Acid. Res., 20:1425
25 (1992). Transformed cells were then inoculated from agar into YEPD complex media broth (100 ml) and grown overnight at 30°C. The YEPD broth was prepared as described in Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Press, Cold Spring Harbor, NY, p. 207 (1994). The overnight culture was then diluted to about 2×10^6 cells/ml (approx. OD₆₀₀=0.1) into fresh YEPD broth (500 ml) and regrown to 1×10^7 cells/ml (approx. OD₆₀₀=0.4-0.5).

30 The cells were then harvested and prepared for transformation by transfer into GS3 rotor bottles in a Sorval GS3 rotor at 5,000 rpm for 5 minutes, the supernatant discarded, and then resuspended into sterile water, and centrifuged again in 50 ml falcon tubes at 3,500 rpm in a Beckman GS-6KR centrifuge. The supernatant was discarded and the cells were subsequently washed with LiAc/TE (10 ml, 10 mM Tris-HCl, 1 mM EDTA pH 7.5, 100 mM Li₂OOCCH₃), and resuspended into LiAc/TE (2.5 ml).

35 Transformation took place by mixing the prepared cells (100 µl) with freshly denatured single stranded salmon testes DNA (Lofstrand Labs, Gaithersburg, MD) and transforming DNA (1 µg, vol. < 10 µl) in microfuge tubes. The mixture was mixed briefly by vortexing, then 40% PEG/TE (600 µl, 40% polyethylene

glycol-4000, 10 mM Tris-HCl, 1 mM EDTA, 100 mM Li₂OOCCH₃, pH 7.5) was added. This mixture was gently mixed and incubated at 30°C while agitating for 30 minutes. The cells were then heat shocked at 42°C for 15 minutes, and the reaction vessel centrifuged in a microfuge at 12,000 rpm for 5-10 seconds, decanted and resuspended into TE (500 µl, 10 mM Tris-HCl, 1 mM EDTA pH 7.5) followed by recentrifugation. The cells were then diluted into TE (1 ml) and aliquots (200 µl) were spread onto the selective media previously prepared in 150 mm growth plates (VWR).

Alternatively, instead of multiple small reactions, the transformation was performed using a single, large scale reaction, wherein reagent amounts were scaled up accordingly.

The selective media used was a synthetic complete dextrose agar lacking uracil (SCD-Ura) prepared as described in Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Press, Cold Spring Harbor, NY, p. 208-210 (1994). Transformants were grown at 30°C for 2-3 days.

The detection of colonies secreting amylase was performed by including red starch in the selective growth media. Starch was coupled to the red dye (Reactive Red-120, Sigma) as per the procedure described by Biely et al., Anal. Biochem., 172:176-179 (1988). The coupled starch was incorporated into the SCD-Ura agar plates at a final concentration of 0.15% (w/v), and was buffered with potassium phosphate to a pH of 7.0 (50-100 mM final concentration).

The positive colonies were picked and streaked across fresh selective media (onto 150 mm plates) in order to obtain well isolated and identifiable single colonies. Well isolated single colonies positive for amylase secretion were detected by direct incorporation of red starch into buffered SCD-Ura agar. Positive colonies were determined by their ability to break down starch resulting in a clear halo around the positive colony visualized directly.

4. Isolation of DNA by PCR Amplification

When a positive colony was isolated, a portion of it was picked by a toothpick and diluted into sterile water (30 µl) in a 96 well plate. At this time, the positive colonies were either frozen and stored for subsequent analysis or immediately amplified. An aliquot of cells (5 µl) was used as a template for the PCR reaction in a 25 µl volume containing: 0.5 µl KlenTaq (Clontech, Palo Alto, CA); 4.0 µl 10 mM dNTP's (Perkin Elmer-Cetus); 2.5 µl KlenTaq buffer (Clontech); 0.25 µl forward oligo 1; 0.25 µl reverse oligo 2; 12.5 µl distilled water. The sequence of the forward oligonucleotide 1 was:

5'-TGTAACGACGGCCAGTTAAATAGACCTGCAATTATTAATCT-3' (SEQ ID NO:1)

The sequence of reverse oligonucleotide 2 was:

5'-CAGGAAACAGCTATGACCACCTGCACACCTGCAAATCCATT-3' (SEQ ID NO:2)

PCR was then performed as follows:

- | | | |
|----|--------------|------------------|
| a. | Denature | 92°C, 5 minutes |
| b. | 3 cycles of: | |
| | Denature | 92°C, 30 seconds |
| | Anneal | 59°C, 30 seconds |
| | Extend | 72°C, 60 seconds |
| c. | 3 cycles of: | |
| | Denature | 92°C, 30 seconds |
| | Anneal | 57°C, 30 seconds |

		Extend	72°C, 60 seconds
d.	25 cycles of:	Denature	92°C, 30 seconds
		Anneal	55°C, 30 seconds
		Extend	72°C, 60 seconds
e.		Hold	4°C

The underlined regions of the oligonucleotides annealed to the ADH promoter region and the amylase region, respectively, and amplified a 307 bp region from vector pSST-AMY.0 when no insert was present. Typically, the first 18 nucleotides of the 5' end of these oligonucleotides contained annealing sites for the sequencing primers. Thus, the total product of the PCR reaction from an empty vector was 343 bp. However, signal sequence-fused cDNA resulted in considerably longer nucleotide sequences.

Following the PCR, an aliquot of the reaction (5 µl) was examined by agarose gel electrophoresis in a 1% agarose gel using a Tris-Borate-EDTA (TBE) buffering system as described by Sambrook et al., *supra*. Clones resulting in a single strong PCR product larger than 400 bp were further analyzed by DNA sequencing after purification with a 96 Qiaquick PCR clean-up column (Qiagen Inc., Chatsworth, CA).

EXAMPLE 3: Isolation of cDNA Clones Using Signal Algorithm Analysis

Various polypeptide-encoding nucleic acid sequences were identified by applying a proprietary signal sequence finding algorithm developed by Genentech, Inc. (South San Francisco, CA) upon ESTs as well as clustered and assembled EST fragments from public (e.g., GenBank) and/or private (LIFESEQ®, Incyte Pharmaceuticals, Inc., Palo Alto, CA) databases. The signal sequence algorithm computes a secretion signal score based on the character of the DNA nucleotides surrounding the first and optionally the second methionine codon(s) (ATG) at the 5'-end of the sequence or sequence fragment under consideration. The nucleotides following the first ATG must code for at least 35 unambiguous amino acids without any stop codons. If the first ATG has the required amino acids, the second is not examined. If neither meets the requirement, the candidate sequence is not scored. In order to determine whether the EST sequence contains an authentic signal sequence, the DNA and corresponding amino acid sequences surrounding the ATG codon are scored using a set of seven sensors (evaluation parameters) known to be associated with secretion signals. Use of this algorithm resulted in the identification of numerous polypeptide-encoding nucleic acid sequences.

EXAMPLE 4: Isolation of cDNA clones Encoding Human PRO1560

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA17409. Based on the DNA17409 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1560.

DNA sequencing of the isolated clones isolated as described above gave the full-length DNA sequence for DNA19902-1669 [Figure 1, SEQ ID NO:3]; and the derived protein sequence for PRO1560.

The entire coding sequence of DNA19902-1669 is included in Figure 1 (SEQ ID NO:3). Clone

DNA19902-1669 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 41-43, and an apparent stop codon at nucleotide positions 776-778. The predicted polypeptide precursor is 245 amino acids long. The approximate locations of the signal peptide, transmembrane domains, N-glycosylation sites, N-myristoylation sites, tyrosine kinase phosphorylation sites, and membrane lipoprotein lipid attachment sites are also indicated in Figure 2. Clone DNA19902-1669 has been deposited with the ATCC and is assigned ATCC deposit no. 203454. The full-length PRO1560 protein shown in Figure 2 has an estimated molecular weight of about 27,563 daltons and a pI of about 8.36.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 2 (SEQ ID NO:4), revealed sequence identity between the PRO1560 amino acid sequence and the following Dayhoff sequences: AF053453_1, AF053454_1, A15_HUMAN, AF054840_1, CD63_HUMAN, AF065389_1, AF054838_1, AF089749_1, P_R27525, and P_R86834.

EXAMPLE 5: Isolation of cDNA clones Encoding Human PRO444

A cDNA sequence isolated in the amylase screen described in Example 2 above was designated DNA13121. Based upon this sequence, probes were generated and used to screen a human fetal lung library (LIB25) prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 608-610 and ending at the stop codon found at nucleotide positions 959-961 (Figure 3, SEQ ID NO:5). The predicted polypeptide precursor is 117 amino acids long, has a calculated molecular weight of approximately 12,692 daltons and an estimated pI of approximately 7.50. Analysis of the full-length PRO444 sequence shown in Figure 4 (SEQ ID NO:6) evidences the presence of a signal peptide at amino acid 1 to about amino acid 16. An analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO444 amino acid sequence and the following Dayhoff sequences: CEF44D12_8, P_R88452, YNE1_CAEEL, A47312, AF009957_1, and A06133_1. Clone DNA26846-1397 was deposited with the ATCC on October 27, 1998 and is assigned ATCC deposit no. 203406.

EXAMPLE 6: Isolation of cDNA clones Encoding Human PRO1018

A cDNA clone (DNA56107-1415) encoding a native human PRO1018 polypeptide was identified by a yeast screen, in a human ovary tumor cDNA library that preferentially represents the 5' ends of the primary cDNA clones. The yeast screen employed identified a single EST clone designated herein as DNA41000. The DNA41000 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into

a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is herein designated DNA44449. Oligonucleotide primers based upon the DNA44449 sequence were then synthesized and employed to screen a human ovary tumor cDNA library which resulted in the identification of the DNA56107-1415 clone shown in Figure 5.

5 The full-length DNA56107-1415 clone shown in Figure 5 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 129-131 and ending at the stop codon at nucleotide positions 696-698 (Figure 5). The predicted polypeptide precursor is 189 amino acids long (Figure 6). Analysis of the full-length PRO1018 sequence shown in Figure 6 (SEQ ID NO:8) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, transmembrane domains from about amino acid 86 to about amino acid 103 and from about amino acid 60 to about amino acid 75 and an amino acid sequence
10 block having homology to G-protein coupled receptor proteins from about amino acid 44 to about amino acid 84. Clone DNA56107-1415 has been deposited with ATCC on October 27, 1998 and is assigned ATCC deposit no. 203405.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 6 (SEQ ID NO:8), evidenced significant
15 homology between the PRO1018 amino acid sequence and the following Dayhoff sequences: CEB0399_4, S59764, YHDT_HAEIN and AE000675_3.

EXAMPLE 7: Isolation of cDNA clones Encoding Human PRO1773

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described
20 in Example 1 above. This consensus sequence is herein designated DNA49797. Based upon an observed homology between the DNA49797 consensus sequence and an EST sequence contained within Incyte EST clone no. 509434, Incyte EST clone no. 509434 was purchased and its insert obtained and sequenced. That sequence is herein shown in Figure 7 and is designated DNA56406-1704.

The entire nucleotide sequence of DNA56406-1704 is shown in Figure 7 (SEQ ID NO:9). Clone
25 DNA56406-1704 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 111-113 and ending at the stop codon at nucleotide positions 1068-1070 (Figure 7). The predicted polypeptide precursor is 319 amino acids long (Figure 8). The full-length PRO1773 protein shown in Figure 8 has an estimated molecular weight of about 35,227 daltons and a pI of about 8.97. Analysis of the full-length PRO1773 sequence shown in Figure 8 (SEQ ID NO:10) evidences the presence of the following: a signal peptide
30 from about amino acid 1 to about amino acid 17, a transmembrane domain from about amino acid 136 to about amino acid 152, potential N-glycosylation sites from about amino acid 161 to about amino acid 164, from about amino acid 187 to about amino acid 190 and from about amino acid 253 to about amino acid 256, a glycosaminoglycan attachment site from about amino acid 39 to about amino acid 42 and potential N-myristolation sites from about amino acid 36 to about amino acid 41, from about amino acid 42 to about amino
35 acid 47, from about amino acid 108 to about amino acid 113, from about amino acid 166 to about amino acid 171, from about amino acid 198 to about amino acid 203 and from about amino acid 207 to about amino acid 212. Clone DNA56406-1704 has been deposited with ATCC on November 17, 1998 and is assigned ATCC

deposit no. 203478.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 8 (SEQ ID NO:10), evidenced significant homology between the PRO1773 amino acid sequence and the following Dayhoff sequences: ROH2_RAT, ROH3_RAT, AF030513_1, ROH1_RAT, AF056194_1, AF057034_1, P_W18337, P_W18328, BDH_HUMAN
5 and BDH_RAT.

EXAMPLE 8: Isolation of cDNA clones Encoding Human PRO1477

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA52641. Based on the DNA52641
10 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO240.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CGCCAGAAGGGCGTGATTGACGTC-3' (SEQ ID NO:13)
15 reverse PCR primer 5'-CCATCCTTCTTCCCAGACAGGCCG-3' (SEQ ID NO:14)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA52641 sequence which had the following nucleotide sequence

hybridization probe

5'-GAAGCCTGTGTCCAGGTCCTTCAGTGAGTGGTTTGGCCTCGGTC-3' (SEQ ID NO:15)

20 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO240 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for
25 PRO1477 (designated herein as DNA56529-1647 [Figure 9, SEQ ID NO:11]; and the derived protein sequence for PRO1477.

The entire nucleotide sequence of DNA56529-1647 is shown in Figure 9 (SEQ ID NO:11). Clone DNA56529-1647 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 23-25 and ending at the stop codon at nucleotide positions 2120-2122 (Figure 9). The predicted
30 polypeptide precursor is 699 amino acids long (Figure 10). The full-length PRO240 protein shown in Figure 10 has an estimated molecular weight of about 79,553 daltons and a pI of about 7.83. Analysis of the full-length PRO1477 sequence shown in Figure 10 (SEQ ID NO:12) evidences the presence of the following: transmembrane domains from about amino acid 21 to about amino acid 40 and from about amino acid 84 to about amino acid 105. Clone DNA56529-1647 has been deposited with ATCC on September 29, 1998 and is assigned
35 ATCC deposit no. 203293.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 10 (SEQ ID NO:12), evidenced significant

homology between the PRO1477 amino acid sequence and the following Dayhoff sequences: CELT03G11_1, CEZC410_4, A54408, SS MAN9MAN_1, GEN12643, GEN12642, AF027156_1, P_W46900, SPAC23A1_4 and DMC86E4_5.

EXAMPLE 9: Isolation of cDNA clones Encoding Human PRO1478

5 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "DNA52719". Based on the DNA52719 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1478.

10 PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'GCGAACGCTTCGAGGAGTCCTGG3' (SEQ ID NO:18); and

reverse PCR primer 5'GCAGTGCGGGAAGCCACATGGTAC3' (SEQ ID NO:19).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensusDNA52719 sequence which had the following nucleotide sequence:

15 hybridization probe 5'CTTCCTGAGCAGGAAGAAGATCCGGCACCACATCTACGTGCTCAAC3' (SEQ ID NO:20).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1478 gene using the probe oligonucleotide and one of the PCR primers. RNA
20 for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1478 and the derived protein sequence for PRO1478.

The entire coding sequence of PRO1478 is included in Figure 11 (SEQ ID NO:16). Clone DNA56531-1648 contains a single open reading frame with an apparent translational initiation site at nucleotide positions
25 77-79 and an apparent stop codon at nucleotide positions 1058-1060 of SEQ ID NO:16. The predicted polypeptide precursor is 327 amino acids long. The type II transmembrane sequence is believed to be at about amino acids 29-49 of SEQ ID NO:17, and an N-glycosylation site is believed to be at about amino acids 154-157 of SEQ ID NO:17. Clone DNA56531-1648 has been deposited with ATCC and is assigned ATCC deposit no. 203286. The full-length PRO1478 protein shown in Figure 12 has an estimated molecular weight of about
30 37,406 daltons and a pI of about 9.3.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 12 (SEQ ID NO:17), revealed sequence identity between the PRO1478 amino acid sequence and the following Dayhoff sequences: YNJ4_CAEEL, P_R55706, A38781_1, NALS_MOUSE, HUMHGT_1, AF048687_1, CEW02B12_11, Y09F_MYCTU, FOJO_DROME,
35 and G01936.

EXAMPLE 10: Isolation of cDNA clones Encoding Human PRO831

DNA56862-1343 was identified by applying the proprietary signal sequence finding algorithm described in Example 3 above. Use of the above described signal sequence algorithm allowed identification of an EST cluster sequence from the Incyte database, designated Incyte cluster sequence no. 25507. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington).

10 The consensus sequence obtained therefrom is herein designated as DNA55714.

In light of the sequence homology between the DNA55714 sequence and an EST sequence contained within the Merck EST clone no. AA099445, the Merck EST clone no. AA099445 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 13 and is herein designated as DNA56862-1343.

15 Clone DNA56862-1343 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 40-42 and ending at the stop codon at nucleotide positions 259-261 (Figure 13). The predicted polypeptide precursor is 73 amino acids long (Figure 14). The full-length PRO831 protein shown in Figure 14 has an estimated molecular weight of about 7,879 daltons and a pI of about 7.21. Analysis of the full-length PRO831 sequence shown in Figure 14 (SEQ ID NO:22) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15 and an amino acid sequence block having homology to growth factor and cytokine receptor family proteins from about amino acid 3 to about amino acid 18. Clone DNA56862-1343 has been deposited with ATCC on September 1, 1998 and is assigned ATCC deposit no. 203174.

25 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 14 (SEQ ID NO:22), evidenced significant homology between the PRO831 amino acid sequence and the following Dayhoff sequences: P_W30724, HUMPPA_1, AF022238_1, 4HHB_C, P_R39727, P_R39728, TRYT_MERUN, GPR5_HUMAN, AB010266_3 and HSBCL3S2_1.

30 EXAMPLE 11: Isolation of cDNA clones Encoding Human PRO1113

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "DNA34025". Based on the DNA34025 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1113.

PCR primers (forward and reverse) were synthesized:
forward PCR primer 5'GAGGACTCACCAATCTGGTTCGGC3' (SEQ ID NO:25); and

reverse PCR primer 5'AACTGGAAAGGAAGGCTGTCTCCC3' (SEQ ID NO:26).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA34025 sequence which had the following nucleotide sequence:

hybridization probe 5'GTAAAGGAGAAGAACATCACGGTACGGGATACCAGGTGTGTTTATCCTAA3' (SEQ ID NO:27).

5 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1113 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1113 (designated herein as DNA57254-1477 [Figure 15, SEQ ID NO:23]; and the derived protein sequence for PRO1113.

The entire coding sequence of PRO1113 is shown in Figure 15 (SEQ ID NO:23). Clone DNA57254-1477 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 214-216, and an apparent stop codon at nucleotide positions 2062-2064 of SEQ ID NO:23. The predicted polypeptide precursor is 616 amino acids long. The transmembrane domain (type II) is believed to be at about amino acids 13-40 of SEQ ID NO:24. The N-glycosylation sites and N-myristoylation sites are indicated in Figure 16. Clone DNA57254-1477 has been deposited with the ATCC and is assigned ATCC deposit no. 203289. The full-length PRO1113 protein shown in Figure 16 has an estimated molecular weight of about 68,243 daltons and a pI of about 8.66.

20 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 16 (SEQ ID NO:24), revealed sequence identity between the PRO1113 amino acid sequence and the following Dayhoff sequences (data incorporated herein): D86983_1, A58532, SLIT_DROME, AB007865_1, AC004142_1, CELT21D12_8, AB003184_1, DMU42767_1, MUSLRRP_1 and GPCR_LYMST.

25

EXAMPLE 12: Isolation of cDNA clones Encoding Human PRO1194

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from a human pineal gland library. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56511.

In light of the sequence homology between the DNA56511 sequence and an EST contained within the

Merck EST AA069568, the clone 382736 which includes this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 17 and is herein designated as DNA57841-1522.

5 The full length clone shown in Figure 17 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 9-11 and ending at the stop codon found at nucleotide positions 252-254 (Figure 17; SEQ ID NO:28). The predicted polypeptide precursor (Figure 18, SEQ ID NO:29) is 81 amino acids long. The signal peptide is at about amino acids 1-21 of SEQ ID NO:29. PRO1194 has a calculated molecular weight of approximately 9,223 daltons and an estimated pI of approximately 10.47. Clone DNA57841-1522 was deposited with the ATCC on November 3, 1998 and is assigned ATCC deposit no. 203458.

10 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 18 (SEQ ID NO:29), revealed sequence identity between the PRO1194 amino acid sequence and the following Dayhoff sequences: PT17_YEAST, RR2_CHLVU, CEK12F2_1, S22452, S76705, AF031898_7, A4_DROME, AF038931_1, E49905, and GSPL_AERHY.

15

EXAMPLE 13: Isolation of cDNA clones Encoding Human PRO1110

A cDNA clone (DNA58727-1474) encoding a native human PRO1110 polypeptide was identified by a yeast screen, in a human fetal kidney cDNA library that preferentially represents the 5' ends of the primary cDNA clones. The yeast screen employed identified a single EST clone designated herein as DNA45566. The DNA45566 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is herein designated DNA46965. Oligonucleotide primers based upon the DNA46965 sequence were then synthesized and employed to screen a human SK-Lu-1 adenocarcinoma cDNA library (LIB247) which resulted in the identification of the DNA58727-1474 clone shown in Figure 19.

30 The full-length DNA58727-1474 clone shown in Figure 19 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 131-133 and ending at the stop codon at nucleotide positions 1097-1099 (Figure 19). The predicted polypeptide precursor is 322 amino acids long (Figure 20). The full-length PRO1110 protein shown in Figure 20 has an estimated molecular weight of about 35,274 daltons and a pI of about 8.57. Analysis of the full-length PRO1110 sequence shown in Figure 20 (SEQ ID NO:31) evidences the presence of the following: transmembrane domains from about amino acid 41 to about amino acid 60, from about amino acid 66 to about amino acid 85, from about amino acid 101 to about amino acid 120, from about amino acid 137 to about amino acid 153, from about amino acid 171 to about amino acid 192, from about amino acid 205 to about amino acid 226, from about amino acid 235 to about amino acid 255 and from about

amino acid 294 to about amino acid 312, a potential N-glycosylation site from about amino acid 6 to about amino acid 69, and a glycosaminoglycan attachment site from about amino acid 18 to about amino acid 21. Clone DNA58727-1474 has been deposited with ATCC on September 1, 1998 and is assigned ATCC deposit no. 203171.

5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 20 (SEQ ID NO:31), evidenced significant homology between the PRO1110 amino acid sequence and the following Dayhoff sequences: MMYELUPR_1, P_R99799, MAL_HUMAN, P_P80929, RNMALGENE_1, S68406, PLLP_RAT, MMMALPROT_1, I38891 and S55622.

10 EXAMPLE 14: Isolation of cDNA clones Encoding Human PRO1378

An initial DNA sequence referred to herein as DNA51941 was identified using a yeast screen, in a human bone marrow cDNA library that preferentially represents the 5' ends of the primary cDNA clones. Based on the DNA51941 sequence, the following oligonucleotides were synthesized for use as probes to isolate a clone of the full-length coding sequence for PRO1377 from a bone marrow cDNA library:

15 T G T C C T T T G T C C C A G A C T T C T G T C C (SEQ ID NO:34),
 CTGGATGCTAATGTGTCCAGTAAATGATCCCCTTATCCCGTCGCGATGCT (SEQ ID NO:35);
 TTCCACTCAATGAGGTGAGCCACTC (SEQ ID NO:36); GGCGAGCCCTAACTATCCAGGAG (SEQ ID
 NO:37); GGAGATCGCTGCGCTGGCCAGGTCCTCCCTGCATGGTAT (SEQ ID NO:38); and
 CTGCTGCAAAGCGAGCCTCTTG (SEQ ID NO:39).

20 The full length DNA58730-1607 clone shown in Figure 21 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 1365 to 1367 and ending at the stop codon found at nucleotide positions 2370 to 2372 (Figure 21; SEQ ID NO:32). The predicted polypeptide precursor (Figure 22, SEQ ID NO:33) is 335 amino acids long, with a signal peptide sequence at about amino acids 1-15. PRO1378 has a calculated molecular weight of approximately 36,108 daltons and an estimated pI of

25 approximately 4.51.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 22 (SEQ ID NO:33), revealed some homology between the PRO1378 amino acid sequence and the following Dayhoff sequences: ICAL_RABIT, SP2_HUMAN, SHPSRBB_1, SP23_HUMAN, P_W08158, and P_W08150.

30 Clone DNA58730-1607 was deposited with the ATCC on September 15, 1998, and is assigned ATCC deposit no. 203221.

EXAMPLE 15: Isolation of cDNA clones Encoding Human PRO1481

35 An initial DNA sequence, referred to herein as DNA53254, was identified using a yeast screen, in a human fetal kidney cDNA library that preferentially represents the 5' ends of the primary cDNA clones. Based on the DNA53254 sequence, oligonucleotides were synthesized for use as probes (or primers) to isolate a clone of the full-length coding sequence for PRO1481 from a human fetal kidney cDNA library.

The full length DNA58732-1650 clone shown in Figure 23 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 320-322 and ending at the stop codon found at nucleotide positions 1322-1324 (Figure 23; SEQ ID NO:40). The predicted polypeptide precursor (Figure 24, SEQ ID NO:41) is 334 amino acids long. The signal peptide is at about amino acids 1-23, and a transmembrane domain is at about amino acids 235-262 of SEQ ID NO:41. The N-glycosylation sites are indicated in Figure 24. PRO1481 has a calculated molecular weight of approximately 36,294 daltons and an estimated pI of approximately 4.98. Clone DNA58732-1650 has been deposited with the ATCC and is assigned ATCC deposit no. 203290.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 24 (SEQ ID NO:41), revealed sequence identity between the PRO1481 amino acid sequence and the following Dayhoff sequences (data incorporated herein): YN23_YEAST, S67770, H36857, YLU2_PICAN, GEN12881, CVY15035_28, YM96_YEAST, ESC1_SCHPO, CELZK783_1 and S59310.

EXAMPLE 16: Isolation of cDNA clones Encoding Human PRO1189

A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated DNA41784. The DNA41784 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and proprietary EST DNA databases (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA; and Genentech, South San Francisco, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA45499.

Based on the DNA45499 sequence, oligonucleotide probes were generated and used to screen a human bone marrow library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (45499.f1) 5'-GAAAGACACGACACAGCAGCTTGC-3' (SEQ ID NO:44)
forward PCR primer (45499.f2) 5'-GGGAACTGCTATCTGATGCC-3' (SEQ ID NO:45)
forward PCR primer (45499.f3) 5'-CAGGATCTCCTCTTGCAGTCTGCAGC-3' (SEQ ID NO:46)
reverse PCR primer (45499.r1) 5'-CTTCTCGAACCACATAAGTTTGAGGCAG-3' (SEQ ID NO:47)
reverse PCR primer (45499.r2) 5'-CACGATTCCCTCCACAGCAACTGGG-3' (SEQ ID NO:48).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA45499 sequence which had the following nucleotide sequence:

hybridization probe (45499.p1)

5'-CGCCTTACCGCGCAGCCCGAAGATTCACTATGGTGAAAATCGCCTTCAAT-3' (SEQ ID NO:49).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1189 gene using the probe oligonucleotide and one of the PCR primers.

5 A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 79-81, and a stop signal at nucleotide positions 868-870 (Figure 25; SEQ ID NO:42). The predicted polypeptide precursor is 263 amino acids long has a calculated molecular weight of approximately 29,741 daltons and an estimated pI of approximately 5.74. Additional features include a type II transmembrane domain at about amino acids 53-75 and a potential N-glycosylation site at about amino acids 166-169.

10 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 26 (SEQ ID NO:43), evidenced significant homology between the PRO1189 amino acid sequence and Dayhoff sequences MUSE25A_1 and HS696H22_1. Additionally, some homology was revealed between the PRO1189 amino acid sequence and the following Dayhoff sequences: AF017985_1, CBRG01D9_2, I79662, and CHPDRBAG_1.

15 Clone DNA58828-1519 has been deposited with ATCC and is assigned ATCC deposit no. 203172.

EXAMPLE 17: Isolation of cDNA clones Encoding Human PRO1415

20 Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 150918. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, 25 Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55720.

In light of the sequence homology between the DNA55720 sequence and an EST sequence contained within the Incyte EST clone no. 4081476, the Incyte EST clone no. 4081476 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 27 and is herein designated as DNA58852-1637.

30 Clone DNA58852-1637 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 148-150 and ending at the stop codon at nucleotide positions 997-999 (Figure 27). The predicted polypeptide precursor is 283 amino acids long (Figure 28). The full-length PRO1415 protein shown in Figure 28 has an estimated molecular weight of about 29,191 daltons and a pI of about 4.52. Analysis of the full-length PRO1415 sequence shown in Figure 28 (SEQ ID NO:50) evidences the presence of the 35 following: a signal peptide from about amino acid 1 to about amino acid 25, a transmembrane domain from about amino acid 94 to about amino acid 118 and potential N-myristoylation sites from about amino acid 18 to about amino acid 23, from about amino acid 40 to about amino acid 45, from about amino acid 46 to about amino acid

51, from about amino acid 145 to about amino acid 150, from about amino acid 192 to about amino acid 197, from about amino acid 193 to about amino acid 198, from about amino acid 211 to about amino acid 216, from about amino acid 238 to about amino acid 243 and from about amino acid 242 to about amino acid 247. Clone DNA58852-1637 has been deposited with ATCC on September 22, 1998 and is assigned ATCC deposit no. 203271.

5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 28 (SEQ ID NO:50), evidenced significant homology between the PRO1415 amino acid sequence and the following Dayhoff sequences: HSU66616_1, P_W24017, A38219, CD30_HUMAN, HSU78971_1, P_W22214, NFM_HUMAN, ADH1_ASPFL, PAU93274_5 and CENB_MOUSE.

10

EXAMPLE 18: Isolation of cDNA clones Encoding Human PRO1411

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from an Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary
15 EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs were derived from a thyroid tissue library. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green,
20 University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56013.

In light of the sequence homology between the DNA56013 sequence and an EST sequence contained within the Incyte EST 1444225, the clone including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 29 and is herein designated as DNA59212-
25 1627.

The full length clone shown in Figure 29 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 184-186 and ending at the stop codon found at nucleotide positions 1504-1506 (Figure 29; SEQ ID NO:51). The predicted polypeptide precursor (Figure 30, SEQ ID NO:52) is 440 amino acids long. The signal peptide is at about amino acids 1-21, and the cell attachment site
30 is at about amino acids 301-303 of SEQ ID NO:52. PRO1411 has a calculated molecular weight of approximately 42,208 daltons and an estimated pI of approximately 6.36. Clone DNA59212-1627 was deposited with the ATCC on September 9, 1998 and is assigned ATCC deposit no. 203245.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 30 (SEQ ID NO:52), revealed sequence identity
35 between the PRO1411 amino acid sequence and the following Dayhoff sequences (data from database incorporated herein): MTV023_19, P_R05307, P_W26348, P_P82962, AF000949_1, EBN1_EBV, P_R95107, GRP2_PHAVU, P_R81318, and S74439_1.

EXAMPLE 19: Isolation of cDNA clones Encoding Human PRO1295

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from a thymus tissue library. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56262.

In light of the sequence homology between the DNA56262 sequence and an EST contained within the Incyte EST 3743334, the clone including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 31 and is herein designated as DNA59218-1559.

The full length clone shown in Figure 31 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 207-209 and ending at the stop codon found at nucleotide positions 1047-1049 (Figure 31; SEQ ID NO:53). The predicted polypeptide precursor (Figure 32, SEQ ID NO:54) is 280 amino acids long. The signal peptide is at about amino acids 1-18 of SEQ ID NO:54. A targeting signal and N-glycosylation site are also indicated in Figure 54. PRO1295 has a calculated molecular weight of approximately 30,163 daltons and an estimated pI of approximately 6.87. Clone DNA59218-1559 was deposited with the ATCC on September 29, 1998 and is assigned ATCC deposit no. 203287.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 32 (SEQ ID NO:54), revealed sequence identity between the PRO1295 amino acid sequence and the following Dayhoff sequences (data incorporated herein): AB011099_1, ILVE_MYCTU, ATTECR_2, AF010496_27, P_R15346, S37191, PER_DROMS, L2MU_ADECC and P_W34238.

EXAMPLE 20: Isolation of cDNA clones Encoding Human PRO1359

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from an Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from a sigmoid colon tissue library. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein

designated DNA56263.

In light of the sequence homology between the DNA56263 sequence and the Incyte EST 1931418, the clone including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 33 and is herein designated as DNA59219-1613.

The full length clone shown in Figure 33 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 184-186 and ending at the stop codon found at nucleotide positions 1081-1083 (Figure 33; SEQ ID NO:55). The predicted polypeptide precursor (Figure 34, SEQ ID NO:56) is 299 amino acids long. The transmembrane domain is at about amino acids 9-31 of SEQ ID NO:56. N-glycosylation sites are at about amino acids 64-67 and 115-118 of SEQ ID NO:56. PRO1359 has a calculated molecular weight of approximately 34,291 daltons and an estimated pI of approximately 9.87. Clone DNA59219-1613 was deposited with the ATCC on September 15, 1998 and is assigned ATCC deposit no. 203220.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 34 (SEQ ID NO:56), revealed sequence identity between the PRO1359 amino acid sequence and the following Dayhoff sequences (data incorporated herein): GEM14384, P_R78622, A23699_1, P_R65244, A54898, AF059321_1, RNU55938_1, BTRNAST6_1, P_R75199 and P_R63216.

EXAMPLE 21: Isolation of cDNA clones Encoding Human PRO1190

The method described in Example 1 above allowed the identification of a single Merck/Washington University EST sequence, EST no. AA339802, which is designated herein as "DNA53943". Based on the DNA53943 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1190.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: (53943.f1) GGGAAACACAGCAGTCATTGCCTGC (SEQ ID NO:59)

reverse PCR primer: (53943.r1) GCACACGTAGCCTGTCGCTGGAGC (SEQ ID NO:60)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA53943 sequence which had the following nucleotide sequence:

hybridization probe: (53943.p1) CACCCCAAAGCCCAGGTCCGGTACAGCGTCAAACAAGAGTGG (SEQ ID NO:61)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1190 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1190 (designated herein as DNA59586-1520 [Figure 35, SEQ ID NO:57]; and the derived protein sequence for PRO1190.

The entire coding sequence of PRO1190 is shown in Figure 35 (SEQ ID NO:57). Clone DNA59586-1520 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 340-342 and an apparent stop codon at nucleotide positions 3685-3687. The predicted polypeptide precursor is 1115 amino acids long. The full-length PRO1190 protein shown in Figure 36 has an estimated molecular weight of about 121,188 daltons and a pI of about 7.07. Other features of the PRO1190 protein include: two transmembrane domains at amino acids 16-30 and 854-879; a cytochrome P450 cystein heme-iron ligand signature at amino acids 1051-1060; an N-6 adenine-specific DNA methylases signature at amino acids 1045-1051; and potential N-glycosylation sites at amino acids 65-68, 76-79, 98-101, 189-192, 275-278, 518-521, 726-729, and 760-763. Clone DNA59586-1520 was deposited with the ATCC on September 29, 1998, and is assigned ATCC deposit no. 203288.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 36 (SEQ ID NO:58), revealed homology between the PRO1190 amino acid sequence and the following Dayhoff sequences: AF004840_1, AF004841_1, AF026465_1, HSU72391_1, P_R13144, AXO1_HUMAN, GEN13349, I58164, D87212_1, A53449, and D86983_1, and KIAA0230.

EXAMPLE 22: Isolation of cDNA clones Encoding Human PRO1772

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA45120. Based on the DNA45120 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1772.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (45120.fl) 5'-CCTTCACCTGCAGTACACCATGGGC-3' (SEQ ID NO:64)

reverse PCR primer (45120.rl) 5'-GTCACACACAGCTCTGGCAGCTGAG-3' (SEQ ID NO:65)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45120 sequence which had the following nucleotide sequence

hybridization probe (45120.pl)

5'-CCAAGTTCAGACACCACATGTACACCAACGTCAGCGGATTGACAAGC-3' (SEQ ID NO:66)

RNA for construction of the cDNA libraries was isolated from human bone marrow tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1772 (designated herein as DNA59817-1703 [Figure 37, SEQ ID NO:62]; and the derived protein sequence for PRO1772.

The entire nucleotide sequence of DNA59817-1703 is shown in Figure 37 (SEQ ID NO:62). Clone DNA59817-1703 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 93-95 and ending at the stop codon at nucleotide positions 1554-1556 (Figure 37). The predicted polypeptide precursor is 487 amino acids long (Figure 38). The full-length PRO1772 protein shown in Figure 38 has an estimated molecular weight of about 53,569 daltons and a pI of about 7.68. Analysis of the full-length

PRO1772 sequence shown in Figure 38 (SEQ ID NO:63) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 36, a transmembrane domain from about amino acid 313 to about amino acid 331, potential N-glycosylation sites from about amino acid 119 to about amino acid 122, from about amino acid 184 to about amino acid 187, from about amino acid 243 to about amino acid 246 and from about amino acid 333 to about amino acid 336, potential N-myristolation sites from about amino acid 41 to about amino acid 46, from about amino acid 59 to about amino acid 64, from about amino acid 73 to about amino acid 78, from about amino acid 133 to about amino acid 138, from about amino acid 182 to about amino acid 187, from about amino acid 194 to about amino acid 199, from about amino acid 324 to about amino acid 329, from about amino acid 354 to about amino acid 359, from about amino acid 357 to about amino acid 362, from about amino acid 394 to about amino acid 399, from about amino acid 427 to about amino acid 432 and from about amino acid 472 to about amino acid 477 and a prokaryotic membrane lipoprotein lipid attachment site from about amino acid 136 to about amino acid 146. Clone DNA59817-1703 has been deposited with ATCC on November 17, 1998 and is assigned ATCC deposit no. 203470.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 38 (SEQ ID NO:63), evidenced significant homology between the PRO1772 amino acid sequence and the following Dayhoff sequences: P_R30823, MDP1_PIG, MDP1_HUMAN, P_R13857, P_R53920, MDP1_MOUSE, P_R30822, JC4222, CELF52C6_2 and MYV027_13.

EXAMPLE 23: Isolation of cDNA clones Encoding Human PRO1248

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 7494. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56056.

In light of the sequence homology between the DNA56056 sequence and an EST contained within the Merck EST clone no. AA404441, the Merck EST clone no. AA404441 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 39 and is herein designated as DNA60278-1530.

Clone DNA60278-1530 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 122-124 and ending at the stop codon at nucleotide positions 671-673 (Figure 39). The predicted polypeptide precursor is 183 amino acids long (Figure 40). The full-length PRO1248 protein shown in Figure 40 has an estimated molecular weight of about 20,574 daltons and a pI of about 6.60. Analysis of the full-length PRO1248 sequence shown in Figure 40 (SEQ ID NO:68) evidences the presence of the

following: a signal peptide from about amino acid 1 to about amino acid 20, a transmembrane domain from about amino acid 90 to about amino acid 112 and potential N-glycosylation sites from about amino acid 21 to about amino acid 24, from about amino acid 38 to about amino acid 41 and from about amino acid 47 to about amino acid 50. Clone DNA60278-1530 has been deposited with ATCC on September 1, 1998 and is assigned ATCC deposit no. 203170.

- 5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 40 (SEQ ID NO:68), evidenced significant homology between the PRO1248 amino acid sequence and the following Dayhoff sequences: AF026198_5, CELR12C12_5, PN0563, S64541_1, PN0564, P_R44881 and XLU78189_1.

10 EXAMPLE 24: Isolation of cDNA clones Encoding Human PRO1316

- The extracellular domain (ECD) which includes the signal sequence, if any, of publicly available databases known to contain secreted sequences were used to search various publicly available EST (Expressed Sequenced Tag) databases (GenBank, Merck/Wash. U). The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology 266: 460-480 (1996)] as a comparison of the ECD
15 protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, WA).

- The above search resulted in the identification of the EST, designated W55979 which showed homology with the secreted protein Dkk-1. The clone corresponding to EST W55979 (clone NbHH19W) was purchased
20 from Merck/Washington University and the cDNA insert was obtained and sequenced in its entirety.

- The nucleic acid sequence corresponding to the full length PRO1316 (designated DNA60608-1577) encoded by the purchased clone, is shown in Figure 41 (SEQ ID NO:69). DNA60608-1577 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 211-213, and a stop codon at nucleotide positions 988-990 (Figure 42; SEQ ID NO:70). The predicted polypeptide precursor is 259 amino
25 acids long. Additional regions of significant interest include the nucleotide residues encoding the signal peptide (211-283), an N-glycosylation site (364-366), and the Zn(2)-Cys(6) binuclear cluster domain (505-655). Clone DNA60608-1577 has been deposited with ATCC and is assigned ATCC deposit no. 203126. The full-length PRO1316 protein shown in Figure 42 has an estimated molecular weight of about 28,447 daltons and a pI of about 9.48.

- 30 Based on a BLAST and FastA sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1316 shows significant amino acid sequence identity to the dickkopf family of proteins. Additionally, DNA60608 has shown homology to AF030433_1, LFE4_CHICK, COL_RABIT, YQI6_CAEEL, ITB6_HUMAN, CONO_LYMST, S41033, D63483_1, D86864_1 and AB001978_1.

35 EXAMPLE 25: Isolation of cDNA clones Encoding Human PRO1197

- An initial DNA sequence, referred to herein as DNA56267, was identified using a yeast screen, in a human SK-Lu-1 adenocarcinoma cDNA library that preferentially represents the 5' ends of the primary cDNA

clones. DNA56267 was used to synthesize oligonucleotides for use as probes to isolate a clone of the full-length coding sequence for PRO1197 from a human breast carcinoma cDNA library.

SEQ ID NO:73: 5'AATTCATGGCAAATATTTCCCTTCCC3' (forward);

SEQ ID NO:74: 5'TGGTAAACTGGCCCAAACTCGG3' (reverse); and

SEQ ID NO:75: 5'TTAAAGTCATCCGTCCTTGGCTCAGGATTTGGAGAGCTTGCACCACCAAA3'

5 (probe).

The full length DNA60611-1524 clone shown in Figure 43 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 311-313 and ending at the stop codon found at nucleotide positions 1400-1402 (Figure 43; SEQ ID NO:71). The predicted polypeptide precursor (Figure 44, SEQ ID NO:72) is 363 amino acids long. The signal peptide is at about amino acids 1-24 of SEQ ID NO:72.

10 PRO1197 has a calculated molecular weight of approximately 38,825 daltons and an estimated pI of approximately 9.88. Clone DNA60611-1524 has been deposited with ATCC and is assigned ATCC deposit no. 203175.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 44 (SEQ ID NO:72), revealed sequence identity

15 between the PRO1197 amino acid sequence and the following Dayhoff sequences (information from database incorporated herein): Y144_HUMAN, I47141 (a gastric mucin, mucins are described in *Ann. NY Acad. Sci.*, 140(2):804-834 (1967), AMYH_YEAST, CELK06A9_3, CELZK783_1, HKR1_YEAST, AB003521_1, D87895_1, S61993 and YM96_YEAST.

20 EXAMPLE 26: Isolation of cDNA clones Encoding Human PRO1293

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 115204. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto,

25 CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56522.

30 In light of the sequence homology between the DNA56522 sequence and an EST contained within the Incyte EST clone no. 2966119, the Incyte EST clone no. 2966119 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 45 and is herein designated as DNA60618-1557.

Clone DNA60618-1557 contains a single open reading frame with an apparent translational initiation

35 site at nucleotide positions 37-39 and ending at the stop codon at nucleotide positions 1060-1062 (Figure 45). The predicted polypeptide precursor is 341 amino acids long (Figure 46). The full-length PRO1293 protein shown in Figure 46 has an estimated molecular weight of about 38,070 daltons and a pI of about 6.88. Analysis

of the full-length PRO1293 sequence shown in Figure 46 (SEQ ID NO:77) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, a transmembrane domain from about amino acid 237 to about amino acid 262, a potential N-glycosylation site from about amino acid 205 to about amino acid 208, a cell attachment sequence from about amino acid 151 to about amino acid 152 and an amino acid sequence block having homology to coproporphyrinogen III oxidase proteins from about amino acid 115 to about amino acid 140. Clone DNA60618-1557 has been deposited with ATCC on September 29, 1998 and is assigned ATCC deposit no. 203292.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 46 (SEQ ID NO:77), evidenced significant homology between the PRO1293 amino acid sequence and the following Dayhoff sequences: HSVCD54_1, A33_HUMAN, AF009220_1, HSU82279_1, AF004230_1, P_R13272, AF004231_1, AF043644_1, S44125 and HSIGGHC85_1.

EXAMPLE 27: Isolation of cDNA clones Encoding Human PRO1380

A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated DNA45776. Based on the DNA45776 sequence, oligonucleotide probes were generated and used to screen a human retina library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (45776.f1) 5'-TTTTGCGGTCACCATTTGTCTGC-3' (SEQ ID NO:80) and reverse PCR primer (45776.r1) 5'-CGTAGGTGACACAGAAGCCCAGG-3' (SEQ ID NO:81).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA45776 sequence which had the following nucleotide sequence:

hybridization probe (45776.p1) 5'-TACGGCATGACCGGCTCCTTTCTATGAGGAACTCCCAGGCACTGATAT-3' (SEQ ID NO:82).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1380 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 36-38, and a stop signal at nucleotide positions 1461-1463 (Figure 47; SEQ ID NO:78). The predicted polypeptide precursor is 470 amino acids long has a calculated molecular weight of approximately 51,715 daltons and an estimated pI of approximately 7.86. Additional features include transmembrane domains at about amino acids 50-74, 105-127, 135-153, 163-183, 228-252, 305-330, and 448-472; potential N-glycosylation sites at about amino acids 14-17 and 84-87; and a dihydrofolate reductase signature at about amino acids 60-68.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 48 (SEQ ID NO:79), evidenced homology

between the PRO1380 amino acid sequence and the following Dayhoff sequences: HSU81375_1, CEZK809_6, CEK02E11_1, AF034102_1, JC4196, CEF36H2_2, P_R92315, YAC2_YEAST, F1707_13, and CEF44D12_3.

Clone DNA60740-1615 was deposited with the ATCC on November 3, 1998, and is assigned ATCC deposit no. 203456.

5 EXAMPLE 28: Isolation of cDNA clones Encoding Human PRO1265

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated EST Cluster No. 86995. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to
10 identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs used in the assembly was derived from a cDNA library prepared
15 from RNA isolated from inflamed human adenoid tissue. The consensus sequence obtained therefrom is herein designated DNA55717.

In light of the sequence homology between the DNA55717 sequence and an EST sequence contained within Incyte EST no. 20965, EST clone no. 20965 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 49 and is herein designated as DNA60764.

20 The full length clone shown in Figure 49 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 79-81 and ending at the stop codon found at nucleotide positions 1780-1782 (Figure 49; SEQ ID NO:83). The predicted polypeptide precursor (Figure 50, SEQ ID NO:84) is 567 amino acids long. PRO1265 has a calculated molecular weight of approximately 62,881 daltons and an estimated pI of approximately 8.97. Additional features include a signal peptide sequence at about amino acids
25 1-21; potential N-glycosylation sites at about amino acids 54-57, 134-137, 220-223, and 559-562; and a region having amino acid sequence identity with D-amino acid oxidase proteins at about amino acids 61-80.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 50 (SEQ ID NO:84), revealed significant sequence identity between the PRO1265 amino acid sequence and Dayhoff sequence no. MMU70429_1.
30 Sequence homology was also found to exist between the full-length sequence shown in Figure 50 (SEQ ID NO:84) and the following additional Dayhoff sequences: BC542A_1, E69899, S76290, MTV014_14, AOFB_HUMAN, ZMJ002204_1, S45812_1, DBRNAPD_1, and CRT1_SOYBN.

Clone DNA60764-1533 was deposited with the ATCC on November 10, 1998, and is assigned ATCC deposit no. 203452.

35

EXAMPLE 29: Isolation of cDNA clones Encoding Human PRO1250

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 56523. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56103.

In light of the sequence homology between the DNA56103 sequence and an EST sequence contained within the Incyte EST clone no. 3371784, the Incyte EST clone no. 3371784 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 51 and is herein designated as DNA60775-1532.

Clone DNA60775-1532 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 74-76 and ending at the stop codon at nucleotide positions 2291-2293 (Figure 51). The predicted polypeptide precursor is 739 amino acids long (Figure 52). The full-length PRO1250 protein shown in Figure 52 has an estimated molecular weight of about 82,263 daltons and a pI of about 7.55. Analysis of the full-length PRO1250 sequence shown in Figure 52 (SEQ ID NO:86) evidences the presence of the following: a type II transmembrane domain from about amino acid 61 to about amino acid 80, a putative AMP-binding domain signature sequence from about amino acid 314 to about amino acid 325, and potential N-glycosylation sites from about amino acid 102 to about amino acid 105, from about amino acid 588 to about amino acid 591 and from about amino acid 619 to about amino acid 622. Clone DNA60775-1532 has been deposited with ATCC on September 1, 1998 and is assigned ATCC deposit no. 203173.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 52 (SEQ ID NO:86), evidenced significant homology between the PRO1250 amino acid sequence and the following Dayhoff sequences: LCFB_HUMAN, S56508_1, BNAMPBP2_1, BNACS7_1, CELT08B1_6, CELC46F4_2, AF008206_6, CELR07C3_11, LMU70253_2 and AF008206_7.

EXAMPLE 30: Isolation of cDNA clones Encoding Human PRO1475

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA45639. Based on the DNA45639 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1475.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (45639.f1) 5'-GATGGCAAACGTGTGTTTGACACG-3' (SEQ ID NO:89)
 forward PCR primer (45639.f2) 5'-CCTCAACCAGGCCACGGGCCAC-3' (SEQ ID NO:90)
 reverse PCR primer (45639.r1) 5'-CCCAGGCAGAGATGCAGTACAGGC-3' (SEQ ID NO:91)

reverse PCR primer (45639.r2) 5'-CCTCCAGTAGGTGGATGGATTGGCTC-3' (SEQ ID NO:92)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45639 sequence which had the following nucleotide sequence

hybridization probe (45639.p1)

5'-CTCACCTCATGAGGATGAGGCCATGGTGCTATTCCTCAACATGGTAG-3' (SEQ ID NO:93)

5 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1475 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal brain tissue.

10 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1475 (designated herein as DNA61185-1646 [Figure 53, SEQ ID NO:87]; and the derived protein sequence for PRO1475.

The entire nucleotide sequence of DNA61185-1646 is shown in Figure 53 (SEQ ID NO:87). Clone DNA61185-1646 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 130-132 and ending at the stop codon at nucleotide positions 2110-2112 (Figure 53). The predicted
15 polypeptide precursor is 660 amino acids long (Figure 54). The full-length PRO1475 protein shown in Figure 54 has an estimated molecular weight of about 75,220 daltons and a pI of about 6.76. Analysis of the full-length PRO1475 sequence shown in Figure 54 (SEQ ID NO:88) evidences the presence of the following: a transmembrane domain from about amino acid 38 to about amino acid 55 and a homologous region to mouse GNT1 from about amino acid 229 to about amino acid 660. Clone DNA61185-1646 has been deposited with
20 ATCC on November 17, 1998 and is assigned ATCC deposit no. 203464.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 54 (SEQ ID NO:88), evidenced significant homology between the PRO1475 amino acid sequence and the following Dayhoff sequences: GNT1_MOUSE, CGU65792_1, CGU65791_1, P_R24781, CELF48E3_1, G786_HUMAN, P_W06547, GNT1_CAEEL,
25 219_HUMAN and EF07_MOUSE.

EXAMPLE 31: Isolation of cDNA clones Encoding Human PRO1377

An initial DNA sequence, referred to herein as DNA46892, was identified using a yeast screen, in a human umbilical vein endothelial cell cDNA library that preferentially represents the 5' ends of the primary
30 cDNA clones. Based on the DNA46892 sequence, the following oligonucleotides were synthesized for use as probes to isolate a clone of the full-length coding sequence for PRO1377 from a human fetal kidney cDNA library: GTTGTGGGTGAATAAAGGAGGGCAG (SEQ ID NO:96), CTGTGCTCATGTTTCATGGACAACTG (SEQ ID NO:97), and GGATGATTTCATCTCCATTAGCCTGCTGTCTCTGGCTATGTTGGTGGGAT (SEQ ID NO:98).

35 The full length DNA61608-1606 clone shown in Figure 55 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 149-151 and ending at the stop codon found at nucleotide positions 1070-1072 (Figure 55; SEQ ID NO:94). The predicted polypeptide precursor (Figure 56,

SEQ ID NO:95) is 307 amino acids long. PRO1377 has a calculated molecular weight of approximately 32,251 daltons and an estimated pI of approximately 6.62. Additional features include: a signal peptide at about amino acids 1-18; potential N-glycosylation sites at about amino acids 29-32 and 241-244, and transmembrane domains at about amino acids 37-56, 106-122, 211-230, 240-260, and 288-304.

5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 56 (SEQ ID NO:95), revealed some homology between the PRO1377 amino acid sequence and the following Dayhoff sequences: CET01D3_6, CET28F3_4, CEF26D10_3, S66962, ATX2_YEAST, CEH13N06_8, S49959, YIC3_YEAST, G02273, and P_W35557.

Clone DNA61608-1606 has been deposited with ATCC and is assigned ATCC deposit no. 203239.

10 EXAMPLE 32: Isolation of cDNA clones Encoding Human PRO1326

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte Cluster No. 59366, also referred herein as "DNA10295". This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database
15 (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs was derived from RNA
20 isolated from tumor tissue removed from the penis of a male with squamous cell carcinoma. The consensus sequence obtained therefrom is herein designated DNA56257.

In light of the sequence homology between the DNA56257 sequence and an EST sequence contained within Incyte EST no. 1450878, the EST clone 1450878 was purchased and the cDNA insert was obtained and sequenced in its entirety. The sequence of this cDNA insert is shown in Figure 57 and is herein designated as
25 "DNA62808-1582".

The full length clone shown in Figure 57 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 112 to 114 and ending at the stop codon found at nucleotide positions 1315 to 1317 (Figure 57; SEQ ID NO:99). The predicted polypeptide precursor (Figure 58, SEQ ID NO:100) is 401 amino acids long. Other features of the PRO1326 protein include: a signal sequence at about
30 amino acids 1-29; a ribosomal protein S3Ae homologous region at about amino acids 129-166; and potential N-glycosylation sites at about amino acids 109-112, 144-147 and 398-401. PRO1326 has a calculated molecular weight of approximately 45,333 daltons and an estimated pI of approximately 4.95. Clone DNA62808-1582 was deposited with the ATCC on October 20, 1998 and is assigned ATCC deposit no. 203358.

35 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 58 (SEQ ID NO:100), revealed some homology between the PRO1326 amino acid sequence and the following Dayhoff sequences: AC004013_1, HROMHCMB_1, CEF47A4_2, A45592, MYSP_HUMAN, NFU43192_1, ONGMBWMZ_1, CELC25A11_2,

CELC25A11_1, and A42184.

EXAMPLE 33: Isolation of cDNA clones Encoding Human PRO1249

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster no. 122605. This EST cluster sequence
5 was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and
10 assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56060.

In light of the sequence homology between the DNA56060 sequence and an EST sequence contained within the Incyte EST clone no. 2630770, the Incyte EST clone no. 2630770 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 59 and is herein designated
15 as DNA62809-1531.

Clone DNA62809-1531 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 3-5 and ending at the stop codon at nucleotide positions 3270-3272 (Figure 59). The predicted polypeptide precursor is 1089 amino acids long (Figure 60). The full-length PRO1249 protein shown in Figure 60 has an estimated molecular weight of about 118,699 daltons and a pI of about 8.49. Analysis of
20 the full-length PRO1249 sequence shown in Figure 60 (SEQ ID NO:102) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 16, transmembrane domains from about amino acid position 317 to about amino acid position 341, from about amino acid position 451 to about amino acid position 470, from about amino acid position 481 to about amino acid position 500, from about amino acid position 510 to about amino acid position 527, from about amino acid position 538 to about amino acid position
25 555, from about amino acid position 831 to about amino acid position 850, from about amino acid position 1016 to about amino acid position 1034 and from about amino acid position 1052 to about amino acid position 1070, a leucine zipper pattern sequence from about amino acid 843 to about amino acid 864 and potential N-glycosylation sites from about amino acid 37 to about amino acid 40 and from about amino acid 268 to about amino acid 271. Clone DNA62809-1531 has been deposited with ATCC on September 9, 1998 and is assigned
30 ATCC deposit no. 203237.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 60 (SEQ ID NO:102), evidenced significant homology between the PRO1249 amino acid sequence and the following Dayhoff sequences: AC004472_3, AB004539_7, S64782, S62432, YJG2_YEAST, CELC27A12_8, YKQ5_YEAST, AB009505_3, SPBC24E9_8
35 and AF060218_4.

EXAMPLE 34: Isolation of cDNA clones Encoding Human PRO1315

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA35925. Based on the DNA35925 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1315.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (35925.f1) 5'-CGCTGCTGCTGTTGCTCCTGG-3' (SEQ ID NO:105)

forward PCR primer (35925.f2) 5'-CAGTGTGCCAGGACTTTG-3' (SEQ ID NO:106)

forward PCR primer (35925.f3) 5'-AGTCGCAGGCAGCGTTGG-3' (SEQ ID NO:107)

10 reverse PCR primer (35925.r1) 5'-CTCCTCCGAGTCTGTGTGCTCCTGC-3' (SEQ ID NO:108)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35925 sequence which had the following nucleotide sequence

hybridization probe (35925.p1)

5'-GGACGGGCAGTTCCTGTGTCTCTGGTGGTTTGCCTAAACCTGCAAACATC-3' (SEQ ID NO:109)

15 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1315 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human retina tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1315 (designated herein as DNA62815-1576 [Figure 61, SEQ ID NO:103]; and the derived protein sequence for PRO1315.

The entire nucleotide sequence of DNA62815-1576 is shown in Figure 61 (SEQ ID NO:103). Clone DNA62815-1576 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and ending at the stop codon at nucleotide positions 1447-1449 (Figure 61). The predicted polypeptide precursor is 442 amino acids long (Figure 62). The full-length PRO1315 protein shown in Figure 62 has an estimated molecular weight of about 49,932 daltons and a pI of about 4.55. Analysis of the full-length PRO1315 sequence shown in Figure 62 (SEQ ID NO:104) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, a transmembrane domain from about amino acid 140 to about amino acid 163 and potential N-glycosylation sites from about amino acid 71 to about amino acid 74, from about amino acid 80 to about amino acid 83, from about amino acid 89 to about amino acid 92, from about amino acid 204 to about amino acid 207 and from about amino acid 423 to about amino acid 426. Clone DNA62815-1576 has been deposited with ATCC on September 9, 1998 and is assigned ATCC deposit no. 203247.

35 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 62 (SEQ ID NO:104), evidenced significant homology between the PRO1315 amino acid sequence and the following Dayhoff sequences: MMU53696_1, NVY08571_2, B64560, STMSLPE_1, P_R80508, P_W19258, A55817, GEN14043, AE000768_7 and

RNMUCASGP5_1pSMC.

EXAMPLE 35: Isolation of cDNA clones Encoding Human PRO1599

Incyte EST no. 1491360 was identified as a sequence of interest using the techniques described in Example 1 above having a BLAST score of 70 or greater that does not encode a known protein. The nucleotide
5 sequence of EST no. 1491360 and its complementary sequence is designated herein "DNA37192". Based on the DNA37192 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1599.

PCR primers (forward and reverse) were synthesized:

10 forward PCR primer: GACGTCTGCAACAGCTCCTGGAAG (37192.f1; SEQ ID NO:112)

reverse PCR primer: CGAGAAGGAAACGAGGCCGTGAG (37192.r1; SEQ ID NO:113)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA37192 sequence which had the following nucleotide sequence:

15 hybridization probe: TGACACTTACCATGCTCTGCACCCGCAGTGGGGACAGCCACAGA (SEQ ID NO:114).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1599 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue.

20 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1599 (designated herein as DNA62845-1684 [Figure 63, SEQ ID NO:110]; and the derived protein sequence for PRO1599.

The entire coding sequence of PRO1599 is shown in Figure 63 (SEQ ID NO:110). Clone DNA62845-1684 contains a single open reading frame with an apparent translational initiation site at nucleotide positions
25 69-71 and an apparent stop codon at nucleotide positions 918-920. The predicted polypeptide precursor is 283 amino acids long. The full-length PRO1599 protein shown in Figure 64 has an estimated molecular weight of about 30,350 daltons and a pI of about 9.66. Additional features of PRO1599 include: a signal peptide at about amino acids 1-30; potential N-glycosylation sites at about amino acids 129-132 and 189-192; a potential cAMP and cGMP-dependent protein kinase phosphorylation site at about amino acids 263-266; potential N-
30 myristoylation sites at about amino acids 28-33, 55-60, 174-179, and 236-241; a potential amidation site at about amino acids 144-147; and a serine protease, trypsin family, histidine active site at about amino acids 70-75.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 64 (SEQ ID NO:111), revealed significant homology between the PRO1599 amino acid sequence and the following Dayhoff sequence: CFAD_PIG.
35 Homology was also found between the PRO1599 amino acids sequence and the following additional Dayhoff sequences. CFAD_HUMAN; P_R05421; P_R55757; P_R05772; GRAM_HUMAN; MUSLMET_1; P_P80335; P_R55758; A42048_1; and P_W05383.

Clone DNA62845-1684 was deposited with the ATCC on October 20, 1998 and is assigned ATCC deposit no. 203361.

EXAMPLE 36: Isolation of cDNA clones Encoding Human PRO1430

A DNA sequence designated herein as DNA49433 was obtained as described in Example 1 above. Merck EST no. T49469, which was identified as being an EST of interest from the assembly, was purchased and the cDNA insert was obtained and sequenced in entirety.

DNA sequencing of the clone as described above gave the full-length DNA sequence for PRO1430, which is designated herein as "DNA64842-1632" (SEQ ID NO:115), and the derived protein sequence for PRO1430 (SEQ ID NO:116). Clone DNA64842-1632 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 82-84, and an apparent stop codon at nucleotide positions 1075-1077. The full-length PRO1430 protein shown in Figure 66 has an estimated molecular weight of about 35,932 daltons and a pI of about 8.45. The predicted polypeptide precursor is 331 amino acids long. Additional features include a signal peptide at about amino acids 1-17; a potential N-glycosylation site at about amino acids 171-174, and regions of homology with short chain alcohol dehydrogenase family proteins at about amino acids 29-51, 116-126, 180-217, and 222-230.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 66 (SEQ ID NO:116), revealed significant homology between the PRO1430 amino acid sequence and Dayhoff sequence no. P_W03198. Homology was also found between the PRO1430 amino acid sequence and the following Dayhoff sequences: MTV030_10, MTV037_2, A40116_1, S42651, CEC15H11_6, SPCC736_13, SCU43704_1, S19842, OXIR_STRAT, and OXIR_STRLI.

Clone DNA64842-1632 has been deposited with ATCC and is assigned ATCC deposit no. 203278.

EXAMPLE 37: Isolation of cDNA clones Encoding Human PRO1374

A consensus DNA sequence encoding PRO1374 was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "DNA47357". Based on the DNA47357 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1374.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5' CGGGACAGGAGACCCAGAAAGGG3' (SEQ ID NO:119) and;

reverse PCR primer 5' GGCCAAGTGATCCAAGGCATCTTC3' (SEQ ID NO:120).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47357 sequence which had the following nucleotide sequence:

hybridizationprobe 5'CTGCGGGACCTGACTAGATTCTACGACAAGGTACTTTCTTTGCATGGGG' (SEQ ID NO:121).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1374 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from a human adenocarcinoma cell line.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1374 and the derived protein sequence for PRO1374.

- 5 The entire coding sequence of PRO1374 is shown in Figure 67 (SEQ ID NO:117). Clone DNA64849-1604 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 20-22 and an apparent stop codon at nucleotide positions 1653-1655 of SEQ ID NO:117. The predicted polypeptide precursor is 544 amino acids long. The approximate locations of the signal peptide, N-glycosylation sites, leucine zipper patterns, and ribonucleotide reductase small subunit signature are indicated in Figure 68.
- 10 Clone DNA64849-1604 has been deposited with the ATCC and is assigned ATCC deposit no. 203468. The full-length PRO1374 protein shown in Figure 68 has an estimated molecular weight of about 61,126 daltons and a pI of about 6.4.

- An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 68 (SEQ ID NO:118), revealed sequence identity
- 15 between the PRO1374 amino acid sequence and the following Dayhoff sequences: CEF35G2_4, P_W37046, S44204, CET28D6_1, CET20B3_6, CELC14E2_3, CUAL_CHICK, ATM7J2_3, S74997 and HIVH5994R8_1.

EXAMPLE 38: Isolation of cDNA clones Encoding Human PRO1311

- A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated
- 20 DNA37721. The DNA37721 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and proprietary EST DNA databases (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA; Genentech, South San Francisco, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or
- 25 in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated "DNA48616". Based on the DNA48616 sequence, oligonucleotide probes were generated and used to screen a human aortic endothelial cell library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D
- 30 that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (48616.f1) 5'-ATCATCTATTCCACCGTGTCTGGC-3' (SEQ ID NO:124)

reverse PCR primer (48616.r1) 5'-GACAGAGTGCTCCATGATGATGTCC-3' (SEQ ID NO:125)

- 35 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA48616 sequence which had the following nucleotide sequence:

hybridization probe (48616.p1)

5'-CCTGTCTGTGGGCATCTATGCAGAGGTTGAGCGGCAGAAATATAAAACCC-3' (SEQ ID NO:126)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1311 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 195-197, and a stop signal at nucleotide positions 1077-1079 (Figure 69; SEQ ID NO:122). The predicted polypeptide precursor is 294 amino acids long has a calculated molecular weight of approximately 33,211 daltons and an estimated pI of approximately 5.35. Additional features include: a signal sequence at about amino acids 1-44; possible transmembrane domains at about amino acids 22-42, 57-85, 94-116, and 230-257; potential N-glycosylation sites at about amino acids 118-121, 1899-192, and 230-233; potential tyrosine kinase phosphorylation sites at about amino acids 3-11 and 129-136; potential N-myristoylation sites at about amino acids 80-85, 109-114, 180-185, 218-223, 248-253, 276-281, 285-290, and 287-292; and a cell attachment sequence at about amino acids 3-5.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 70 (SEQ ID NO:123), evidenced some homology between the PRO1311 amino acid sequence and the following Dayhoff sequences: AF065389_1, AF053455_1, CD63_HUMAN, A15_HUMAN, AF043906_1, C151_HUMAN, AF053453_1, AF054838_1, P_R91446, and CD82_HUMAN.

Clone DNA64863-1573 was deposited with the ATCC on September 9, 1998, and is assigned ATCC deposit no. 203251.

EXAMPLE 39: Isolation of cDNA clones Encoding Human PRO1357

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 69537. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56034.

In light of the sequence homology between the DNA56034 sequence and an EST sequence contained within the Incyte EST clone no. 936239, the Incyte EST clone no. 936239 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 71 and is herein designated as DNA64881-1602.

Clone DNA64881-1602 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 74-76 and ending at the stop codon at nucleotide positions 1526-1528 (Figure 71). The predicted polypeptide precursor is 484 amino acids long (Figure 72). The full-length PRO1357 protein

shown in Figure 72 has an estimated molecular weight of about 52,468 daltons and a pI of about 7.14. Analysis of the full-length PRO1357 sequence shown in Figure 72 (SEQ ID NO:128) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21, potential N-glycosylation sites from about amino acid 48 to about amino acid 51, from about amino acid 264 to about amino acid 267 and from about amino acid 401 to about amino acid 404, a glycosaminoglycan attachment site from about amino acid 412 to about amino acid 415 and an amino acid sequence block having homology to the LBP/BPI/CETP family of proteins from about amino acid 407 to about amino acid 457. Clone DNA64881-1602 has been deposited with ATCC on September 9, 1998 and is assigned ATCC deposit no. 203240.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 72 (SEQ ID NO:128), evidenced significant homology between the PRO1357 amino acid sequence and the following Dayhoff sequences: MMU46068_1, S17447, MMU1_1, BPI_RABIT, P_W16808, P_R21844, PSP_MOUSE, HSLBPEX1_1 and BTU79413_1.

EXAMPLE 40: Isolation of cDNA clones Encoding Human PRO1244

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated cluster no. 7874. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA databases (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA; Genentech, South San Francisco, CA) to identify existing homologies. One or more of the ESTs was derived from a library constructed from tissue of the corpus cavernosum. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated "DNA56011".

In light of the sequence homology between the DNA56011 sequence and an EST sequence contained within Incyte EST No. 3202349, the EST clone no. 3202349 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 73 (SEQ ID NO:129) and is herein designated "DNA64883-1526".

The full length clone shown in Figure 73 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 9-11 and ending at the stop codon found at nucleotide positions 1014-1016 (Figure 73; SEQ ID NO:129). The predicted polypeptide precursor (Figure 74, SEQ ID NO:130) is 335 amino acids long. PRO1244 has a calculated molecular weight of approximately 38,037 daltons and an estimated pI of approximately 9.87. Other features include a signal peptide at about amino acids 1-29; transmembrane domains at about amino acids 183-205, 217-237, 271-287, and 301-321; potential N-glycosylation sites at about amino acids 71-74, and 215-218; and a cell attachment sequence at about amino acids 150-152.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

alignment analysis of the full-length sequence shown in Figure 74 (SEQ ID NO:130), revealed homology between the PRO1244 amino acid sequence and the following Dayhoff sequences: AF008554_1, P_485334, G02297, HUMN33S11_1, HUMN33S10_1, YO13_CAEEL, GEN13255, S49758, E70107, and ERP5_MEDSA.

Clone DNA64883-1526 was deposited with the ATCC on September 9, 1998, and is assigned ATCC deposit no. 203253.

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EXAMPLE 41: Isolation of cDNA clones Encoding Human PRO1246

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 56853. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56021.

In light of the sequence homology between the DNA56021 sequence and an EST sequence contained within the Incyte EST clone no. 2481345, the Incyte EST clone no. 2481345 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 75 and is herein designated as DNA64885-1529.

Clone DNA64885-1529 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 119-121 and ending at the stop codon at nucleotide positions 1727-1729 (Figure 75). The predicted polypeptide precursor is 536 amino acids long (Figure 76). The full-length PRO1246 protein shown in Figure 76 has an estimated molecular weight of about 61,450 daltons and a pI of about 9.17. Analysis of the full-length PRO1246 sequence shown in Figure 76 (SEQ ID NO:132) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15, potential N-glycosylation sites from about amino acid 108 to about amino acid 111, from about amino acid 166 to about amino acid 169, from about amino acid 193 to about amino acid 196, from about amino acid 262 to about amino acid 265, from about amino acid 375 to about amino acid 378, from about amino acid 413 to about amino acid 416 and from about amino acid 498 to about amino acid 501 and amino acid sequence blocks having homology to sulfatase proteins from about amino acid 286 to about amino acid 315, from about amino acid 359 to about amino acid 369 and from about amino acid 78 to about amino acid 97. Clone DNA64885-1529 has been deposited with ATCC on November 3, 1998 and is assigned ATCC deposit no. 203457.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 76 (SEQ ID NO:132), evidenced significant homology between the PRO1246 amino acid sequence and the following Dayhoff sequences: P_R51355, CELK09C4_1, BCU44852_1, IDS_HUMAN, G65169, E64903, ARSA_HUMAN, GL6S_HUMAN, HSARSF_1 and GEN12648.

EXAMPLE 42: Isolation of cDNA clones Encoding Human PRO1356

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 44725. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56023.

In light of the sequence homology between the DNA56023 sequence and an EST sequence contained within the Incyte EST clone no. 4071746, the Incyte EST clone no. 4071746 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 77 and is herein designated as DNA64886-1601.

Clone DNA64886-1601 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 122-124 and ending at the stop codon at nucleotide positions 812-814 (Figure 77). The predicted polypeptide precursor is 230 amino acids long (Figure 78). The full-length PRO1356 protein shown in Figure 78 has an estimated molecular weight of about 24,549 daltons and a pI of about 8.56. Analysis of the full-length PRO1356 sequence shown in Figure 78 (SEQ ID NO:134) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, transmembrane domains from about amino acid 82 to about amino acid 102, from about amino acid 117 to about amino acid 140 and from about amino acid 163 to about amino acid 182, a potential N-glycosylation site from about amino acid 190 to about amino acid 193 and an amino acid sequence block having homology to the PMP-22/EMP/MP20 family of proteins from about amino acid 46 to about amino acid 59. Clone DNA64886-1601 has been deposited with ATCC on September 9, 1998 and is assigned ATCC deposit no. 203241.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 78 (SEQ ID NO:134), evidenced significant homology between the PRO1356 amino acid sequence and the following Dayhoff sequences: AB00014_1, AB000712_1, A39484, AF000959_1, AF035814_1, HSU89916_1, MMU19582_1, P_R30059, HUAC004125_1 and PM22_RAT.

EXAMPLE 43: Isolation of cDNA clones Encoding Human PRO1275

A novel secreted molecule, designated herein as DNA57700, was used to BLAST against Incyte's (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) proprietary database and Genbank's public database. Positive clones were identified and used to generate assembly files by seqext program. The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known

proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

A consensus DNA sequence was assembled relative to other EST sequences using repeated cycles of BLAST and phrap. This consensus sequence is designated herein "DNA59572".

Based on the DNA59572 consensus sequence and its relation to sequences identified in the assembly, one of the clones (Incyte clone 2026581) including one of the sequences in the assembly was purchased and sequenced. Incyte clone 2026581 came from a library constructed of RNA from epidermal breast keratinocytes.

The entire coding sequence of PRO1275 is shown in Figure 79 (SEQ ID NO:135). Clone DNA64888-1542 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 37-39 and an apparent stop codon at nucleotide positions 394-396 of SEQ ID NO:135. The predicted polypeptide precursor is 119 amino acids long. The signal peptide is at about amino acids 1-25 of SEQ ID NO:136. Clone DNA64888-1542 has been deposited with ATCC and is assigned ATCC deposit no. 203249. The full-length PRO1275 protein shown in Figure 79 has an estimated molecular weight of about 13,248 daltons and a pI of about 7.78.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 80 (SEQ ID NO:136), revealed sequence identity between the PRO1275 amino acid sequence and the following Dayhoff sequences (information from database incorporated herein): B48151 (Mst98Cb), D86424_1 (high-sulfur keratin protein), P_R79964 (connective tissue growth factor), CHRD_RAT (chordin), MT_DREPO (metallothionein), PL05_PLETR (plectoxins), P_R25156 (Ig antigen), S73732_1 (VLDP), AF025440_1 (OIP4) and P_R32757 (IGF-II).

EXAMPLE 44: Isolation of cDNA clones Encoding Human PRO1274

A novel secreted molecule, designated herein as DNA57700, was used to blast against Incyte's (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) proprietary database and Genbank's public database. Positive clones were identified and used to generate assembly files by seqext program. The search was performed using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)] as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

A consensus DNA sequence was assembled relative to other EST sequences using repeated cycles of BLAST and phrap. This consensus sequence is designated herein "DNA59573".

Based on the DNA59573 consensus sequence and its relation to sequences identified in the assembly, one of the clones (Incyte clone 2623992) including one of the sequences in the assembly was purchased and sequenced. Incyte clone 2623992 came from a library constructed of RNA from epidermal breast keratinocytes.

The entire coding sequence of PRO1274 is shown in Figure 81 (SEQ ID NO:137). Clone DNA64889-1541 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 24-26, and an apparent stop codon at nucleotide positions 354-356 of SEQ ID NO:137. The predicted

polypeptide precursor is 110 amino acids long. The signal peptide is at about 1-24 of SEQ ID NO:138. Conserved regions in the insulin family of proteins and an N-glycosylation site are indicated in Figure 82. Clone DNA64889-1541 has been deposited with ATCC and is assigned ATCC deposit no. 203250. The full-length PRO1274 protein shown in Figure 82 has an estimated molecular weight of about 12,363 daltons and a pI of about 8.31.

- 5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 82 (SEQ ID NO:138), revealed sequence identity between the PRO1274 amino acid sequence and the following Dayhoff sequences (information from database incorporated herein): CEW05B2_9, AF016922_1 (insulin-like growth factor 1), B48151, A53640, BTIGF2REC_1 (insulin-like growth factor 2), HSNF1GEN12_1, TXA3_RADMA (neurotoxin 3),
10 CXM1_CONGE, P_P61301, TXA4_RADMA (neurotoxin 4).

EXAMPLE 45: Isolation of cDNA clones Encoding Human PRO1412

- Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte Cluster No. 101368, also referred herein as
15 "DNA10643". This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not
20 encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs was derived from RNA isolated from fibroblasts of the prostate stroma removed from a male fetus. The consensus sequence obtained therefrom is herein designated "DNA58754".

- In light of the sequence homology between the DNA58754 sequence and an EST sequence contained
25 within EST no. 3597385, the EST clone 3597385 was purchased and the cDNA insert was obtained and sequenced in its entirety. The sequence of this cDNA insert is shown in Figure 83 and is herein designated as "DNA64897-1628".

- The full length clone shown in Figure 83 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 142 to 144 and ending at the stop codon found at nucleotide
30 positions 1075 to 1077 (Figure 83; SEQ ID NO:139). The predicted polypeptide precursor (Figure 84, SEQ ID NO:140) is 311 amino acids long. Other features of the PRO1412 protein include: a signal sequence at about amino acids 1-28; a transmembrane domain at about amino acids 190-216; potential N-glycosylation sites at about amino acids 49-52, 91-94, 108-111, 128-131, 135-138 and 190-193; a tyrosine kinase phosphorylation site at about amino acids 62-69; and a lysosome-associated membrane glycoprotein duplicated domain at about
35 amino acids 183-224. PRO1412 has a calculated molecular weight of approximately 33,908 daltons and an estimated pI of approximately 6.87. Clone DNA64897-1628 was deposited with the ATCC on September 15, 1998, and is assigned ATCC deposit no. 203216.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 84 (SEQ ID NO:140), revealed some homology between the PRO1412 amino acid sequence and the following Dayhoff sequences: I50116, AF035963_1, NCA2_RAT, I61783, P_W07682, MMHC135G15_3, S21461, MMIGL2_1, ONHIGMV9A_1 and MMU70448_1.

5

EXAMPLE 46: Isolation of cDNA clones Encoding Human PRO1557

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST sequence from the Genentech database, designated "DNA58763. This EST sequence was then compared to a variety of expressed sequence tag (EST) databases, which included the EST databases listed above, to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained from the assembly is herein designated "DNA58763".

15 In light of the sequence homology between the DNA58763 sequence and an EST sequence contained within the EST no.2267403, EST no. 2267403 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 85 and is herein designated as DNA64902-1667.

The full length clone shown in Figure 85 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 287 to 289 and ending at the stop codon found at nucleotide positions 1640 to 1642 (Figure 85; SEQ ID NO:141). The predicted polypeptide precursor (Figure 86, SEQ ID NO:142) is 451 amino acids long. PRO1557 has a calculated molecular weight of approximately 49,675 daltons and an estimated pI of approximately 7.15. Additional features include: a signal sequence at about amino acids 1-25; a potential N-glycosylation site at about amino acids 114-117; a potential cAMP and cGMP-dependent protein kinase phosphorylation site at about amino acids 388-41; potential N-myristoylation sites at about amino acids 54-49, 66-71, 146-151, and 367-372; potential amidation sites at about amino acids 36-39 and 205-208; and an ATP/GTP-binding site motif A (P-loop) at about amino acids 151-258.

20 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 86 (SEQ ID NO:142), revealed significant homology between the PRO1557 amino acid sequence and Dayhoff sequence AF034606_1. Homology was also found between the PRO1557 amino acid sequence and the following Dayhoff sequences: P_W31559, AF031230_1, SOG_DROME, CA11_MOUSE, P_R41320, CHRD_RAT, P_W40288, NEL_CHICK, and HSMUC5B_1.

30 Clone DNA64902-1667 was deposited with the ATCC on October 6, 1998, and is assigned ATCC deposit no. 203317.

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EXAMPLE 47: Isolation of cDNA clones Encoding Human PRO1286

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

cluster sequence from the LIFESEQ® database, designated EST Cluster No. 86809. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). ESTs in the assembly included those identified from tumors, cell lines, or diseased tissue. One or more of the ESTs was obtained from a cDNA library constructed from RNA isolated from diseased colon tissue. The consensus sequence obtained therefrom is herein designated DNA58822.

In light of the sequence homology between the DNA58822 sequence and an EST sequence contained within EST no. 1695434, EST clone no. 1695434 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 87 and is herein designated DNA64903-1553 (SEQ ID NO:143).

The full length clone shown in Figure 87 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 93-95 and ending at the stop codon found at nucleotide positions 372-374 (Figure 87; SEQ ID NO:143). The predicted polypeptide precursor (Figure 88, SEQ ID NO:144) is 93 amino acids long, with a signal sequence at about amino acids 1-18. PRO1286 has a calculated molecular weight of approximately 10,111 daltons and an estimated pI of approximately 9.70.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 88 (SEQ ID NO:144), revealed some homology between the PRO1286 amino acid sequence and the following Dayhoff sequences: SR5C_ARATH, CELC17H12_11, MCPD_ENTAE, JQ2283, INVO_LEMCA, P_R07309, ADEVBCAGN_4, AF020947_1, CELT23H2_1, and MDH_STRAR.

Clone DNA64903-1553 was deposited with the ATCC on September 15, 1998 and is assigned ATCC deposit no. 203223.

EXAMPLE 48: Isolation of cDNA clones Encoding Human PRO1294

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 10559. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57203.

In light of the sequence homology between the DNA57203 sequence and an EST sequence contained

within the Incyte EST clone no. 3037763, the Incyte EST clone no. 3037763 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 89 and is herein designated as DNA64905-1558.

Clone DNA64905-1558 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 110-112 and ending at the stop codon at nucleotide positions 1328-1330 (Figure 89).
5 The predicted polypeptide precursor is 406 amino acids long (Figure 90). The full-length PRO1294 protein shown in Figure 90 has an estimated molecular weight of about 46,038 daltons and a pI of about 6.50. Analysis of the full-length PRO1294 sequence shown in Figure 90 (SEQ ID NO:146) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21 and potential N-glycosylation sites from about amino acid 177 to about amino acid 180 and from about amino acid 248 to about amino acid 251.
10 Clone DNA64905-1558 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203233.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 90 (SEQ ID NO:146), evidenced significant homology between the PRO1294 amino acid sequence and the following Dayhoff sequences: I73636,
15 AF028740_1, AB006686S3_1, P_R98225, RNU78105_1, CELC48E7_4, CEF11C3_3, SCP1_MESAU, TPM3_HUMAN and CELK05B2_3.

EXAMPLE 49: Isolation of cDNA clones Encoding Human PRO1347

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described
20 in Example 1 above. This consensus sequence is designated herein "DNA47373". Based on the DNA47373 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1347.

PCR primers (forward and reverse) were synthesized:

25 forward PCR primer 5'GCGTGGTCCACCTCTACAGGGACG3' (SEQ ID NO:149); and
reverse PCR primer 5'GGAAGTGAACCCAGTGCTGACACC3' (SEQ ID NO:150).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47373 sequence which had the following nucleotide sequence:

hybridization probe 5'GCAGATGCCACAGTATCAAGGCAGGACAAAAGTGGTGAAGGATTC3' (SEQ ID
30 NO:151).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1347 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human small intestine.

35 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1347 and the derived protein sequence for PRO1347.

The entire coding sequence of PRO1347 is shown in Figure 91 (SEQ ID NO:147). Clone DNA64950-

1590 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 183-185, and an apparent stop codon at nucleotide positions 1683-1685 of SEQ ID NO:147. The predicted polypeptide precursor is 500 amino acids long. The signal peptide is at about amino acids 1-17 and the transmembrane domain is at about 239-255 of SEQ ID NO:148. Clone DNA64950-1590 has been deposited with ATCC and is assigned ATCC deposit no. 203224. The full-length PRO1347 protein shown in Figure 92
 5 has an estimated molecular weight of about 56,748 daltons and a pI of about 8.5.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 92 (SEQ ID NO:148), revealed sequence identity between the PRO1347 amino acid sequence and the following Dayhoff sequences (data incorporated herein): BUTY_HUMAN, AF033107_1, HSU90142_1, HSU90144_1, HSB73_1, HS111M5_2, RO52_HUMAN,
 10 AF018080_1, HSAJ03147_4, and MOG_MOUSE.

EXAMPLE 50: Isolation of cDNA clones Encoding Human PRO1305

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA38103. Based on the DNA38103
 15 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1305.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (38103.f1) 5'-AACTGCTCTGTGGTTGGAAGCCTG-3' (SEQ ID NO:154)
 20 reverse PCR primer (38103.r1) 5'-CAGTCACATGGCTGACAGACCCAC-3' (SEQ ID NO:155)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA38103 sequence which had the following nucleotide sequence

hybridization probe (38103.p1)

5'-AGGTTATCAGGGGCTTCACTGTGAAACCTGCAAAGAGG-3' (SEQ ID NO:156)

25 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1305 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for
 30 PRO1305 (designated herein as DNA64952-1568 [Figure 93, SEQ ID NO:152]; and the derived protein sequence for PRO1305.

The entire nucleotide sequence of DNA64952-1568 is shown in Figure 93 (SEQ ID NO:152). Clone DNA64952-1568 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 126-128 and ending at the stop codon at nucleotide positions 900-902 (Figure 93). The predicted
 35 polypeptide precursor is 258 amino acids long (Figure 94). The full-length PRO1305 protein shown in Figure 94 has an estimated molecular weight of about 25,716 daltons and a pI of about 8.13. Analysis of the full-length PRO1305 sequence shown in Figure 94 (SEQ ID NO:153) evidences the presence of the following: a signal

peptide from about amino acid 1 to about amino acid 25, potential N-glycosylation sites from about amino acid 30 to about amino acid 33, from about amino acid 172 to about amino acid 175, from about amino acid 195 to about amino acid 198, from about amino acid 208 to about amino acid 211 and from about amino acid 235 to about amino acid 238 and an EGF-like domain cysteine pattern signature sequence from about amino acid 214 to about amino acid 225. Clone DNA64952-1568 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203222.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 94 (SEQ ID NO:153), evidenced significant homology between the PRO1305 amino acid sequence and the following Dayhoff sequences: CET22A3_7, LMA2_MOUSE, AF055580_1, AF016903_1, LMB2_MOUSE, P_R71730, LMB3_MOUSE, LMG1_HUMAN, LMG1_DROME and LMA5_MOUSE. As such, the PRO1305 polypeptide does show homology to laminin and may be a laminin homolog.

EXAMPLE 51: Isolation of cDNA clones Encoding Human PRO1273

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified. This sequence was blasted against public databases and Incyte's database. The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the extracellular domain (ECD) protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

A consensus DNA sequence was assembled relative to other EST sequences using repeated cycles of BLAST and phrap. This consensus sequence is designated herein "DNA60747". Based on the DNA60747 consensus sequence and its relation to a sequence within the assembly of aligned sequences, Incyte clone 3541105 was purchased and sequenced in full. This Incyte clone came from a library constructed of RNA isolated from seminal vesicle tissue.

The entire coding sequence of PRO1273 is shown in Figure 95 (SEQ ID NO:157). Clone DNA65402-1540 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 26-28 and an apparent stop codon at nucleotide positions 515-517 of SEQ ID NO:157. The predicted polypeptide precursor is 163 amino acids long. The signal peptide is at about amino acids 1-20 and the conserved region in lipocalins is at about amino acids 25-36 of SEQ ID NO:158. Clone DNA65402-1540 has been deposited with ATCC and is assigned ATCC deposit no. 203252. The full-length PRO1273 protein shown in Figure 96 has an estimated molecular weight of about 18,045 daltons and a pI of about 4.87.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 96 (SEQ ID NO:158), revealed sequence identity between the PRO1273 amino acid sequence and the following Dayhoff sequences (information from database incorporated herein): PGHD_FELCA (prostaglandin-h2 d-isomerase precursor), S57748 (prostaglandin D synthetase precursor), LIPO_BUFMA (lipocalin precursor), S52354, QSP_CHICK, ECP19_1, LACB_CAPHI,

OLFA_RANPI, D87752_1, and LACB_BOVIN.

EXAMPLE 52: Isolation of cDNA clones Encoding Human PRO1302

A consensus DNA sequence encoding PRO1302 was assembled relative to other EST sequences using repeated cycles of phrap as described in Example 1 above. This consensus sequence is designated herein
5 "DNA28742". Based on the DNA28742 consensus sequence, the assembly from which the consensus sequence was derived and other information and discoveries provided herein, the Incyte clone 3344926 (from a diseased spleen tissue library) was purchased and sequenced in full. Sequencing provided the full-length DNA sequence for PRO1302 and the derived protein sequence for PRO1302.

The entire coding sequence of PRO1302 is shown in Figure 97 (SEQ ID NO:159). Clone DNA65403-
10 1565 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 43-45 and an apparent stop codon at nucleotide positions 1432-1435 of SEQ ID NO:159. The predicted polypeptide precursor is 463 amino acids long. The signal peptide is at about amino acids 1-15 and the transmembrane sequence is at about amino acids 351-370 of SEQ ID NO:160. Clone DNA65403-1565 has been deposited with the ATCC and is assigned ATCC deposit no. 203230. The full-length PRO1302 protein shown
15 in Figure 98 has an estimated molecular weight of about 50,082 daltons and a pI of about 7.3.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 98 (SEQ ID NO:160), revealed sequence identity between the PRO1302 amino acid sequence and the following Dayhoff sequences (data incorporated herein):
D86358_1, D86359_1, S71403_1, MAG_HUMAN, JH0593, MMSIAL2_1, C22A_HUMAN, PGBM_HUMAN,
20 PGBM_HUMAN, LACH_DROME, and KMLS_HUMAN.

EXAMPLE 53: Isolation of cDNA clones Encoding Human PRO1283

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA28753. Based on the DNA28753
25 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1283.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (28753.f1) 5'-GGAGATGAAGACCCTGTTTCCTG-3' (SEQ ID NO:163)
30 forward PCR primer (28753.f11) 5'-GGAGATGAAGACCCTGTTTCCTGGGTG-3' (SEQ ID NO:164)
reverse PCR primer (28753.r1) 5'-GTCCTCCGGAAAGTCCTTATC-3' (SEQ ID NO:165)
reverse PCR primer (28753.r11) 5'-GCCTAGTGTTCTGGGAACGCAGCTTC-3' (SEQ ID NO:166)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA28753 sequence which had the following nucleotide sequence

35 hybridization probe (28753.p1)
5'-CAGGGACCTGGTACGTGAAGGCCATGGTGGTCGATAAGGACTTCCGGAG-3' (SEQ ID NO:167)
hybridization probe (28753.p11)

5'-CTGTCCTTCACCCTGGAGGAGGAGGATATCACAGGGACCTGGTAC-3' (SEQ ID NO:168)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1283 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast tumor tissue.

5 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1283 (designated herein as DNA65404-1551 [Figure 99, SEQ ID NO:161]; and the derived protein sequence for PRO1283.

The entire nucleotide sequence of DNA65404-1551 is shown in Figure 99 (SEQ ID NO:161). Clone DNA65404-1551 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 45-47 and ending at the stop codon at nucleotide positions 555-557 (Figure 99). The predicted polypeptide precursor is 170 amino acids long (Figure 100). The full-length PRO1283 protein shown in Figure 100 has an estimated molecular weight of about 19,457 daltons and a pI of about 9.10. Analysis of the full-length PRO1283 sequence shown in Figure 100 (SEQ ID NO:162) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 17. Clone DNA65404-1551 has been deposited with ATCC on September 9, 1998 and is assigned ATCC deposit no. 203244

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 100 (SEQ ID NO:162), evidenced significant homology between the PRO1283 amino acid sequence and the following Dayhoff sequences: A40464, VEGP_HUMAN, ALL1_CANFA, LALP_TRIVU, S51803, XELPDS_1, LIPO_BUFMA, S52354, QSP_CHICK and ERBP_RAT.

EXAMPLE 54: Isolation of cDNA clones Encoding Human PRO1279

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA30856. Based on the DNA30856 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1279.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (30856.f1) 5'-GGCTGCGGGACTGGAAGTCATCGGG-3' (SEQ ID NO:171)
 30 forward PCR primer (30856.f11) 5'-CTCCAGGCCATGAGGATTCTGCAG-3' (SEQ ID NO:172)
 forward PCR primer (30856.f12) 5'-CCTCTGGTCTGTAACCAG-3' (SEQ ID NO:173)
 reverse PCR primer (30856.r1) 5'-TCTGTGATGTTGCCGGGGTAGGCG-3' (SEQ ID NO:174)
 reverse PCR primer (30856.r11) 5'-CGTGTAGACACCAGGCTTTCGGGTG-3' (SEQ ID NO:175)
 reverse PCR primer (30856.r12) 5'-CCCTTGATGATCCTGGTC-3' (SEQ ID NO:176)
 35 Additionally, synthetic oligonucleotide hybridization probes were constructed from the consensus DNA30856 sequence which had the following nucleotide sequences
 hybridization probe (30856.p1)

5'-AGGCCATGAGGATTCTGCAGTTAATCCTGCTTGCTCTGGCAACAGGGCTT-3' (SEQ ID NO:177)
hybridization probe (30856.p11)

5'-GAGAGACCAGGATCATCAAGGGGTTTCGAGTGCAAGCCTCACTC-3' (SEQ ID NO:178)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1279 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human lung tumor tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1279 (designated herein as DNA65405-1547 [Figure 101, SEQ ID NO:169]; and the derived protein sequence for PRO1279.

The entire nucleotide sequence of DNA65405-1547 is shown in Figure 101 (SEQ ID NO:169). Clone DNA65405-1547 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 106-108 and ending at the stop codon at nucleotide positions 856-858 (Figure 101). The predicted polypeptide precursor is 250 amino acids long (Figure 102). The full-length PRO1279 protein shown in Figure 102 has an estimated molecular weight of about 27,466 daltons and a pI of about 8.87. Analysis of the full-length PRO1279 sequence shown in Figure 102 (SEQ ID NO:170) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 18, a serine protease, trypsin family, histidine active site from about amino acid 58 to about amino acid 63, potential N-glycosylation sites from about amino acid 99 to about amino acid 102, from about amino acid 165 to about amino acid 168, from about amino acid 181 to about amino acid 184 and from about amino acid 210 to about amino acid 213, a glycosaminoglycan attachment site from about amino acid 145 to about amino acid 148, amino acid sequence blocks present in kringle domain proteins from about amino acid 197 to about amino acid 209 and from about amino acid 47 to about amino acid 64, amino acid sequence blocks having homology to serine protease, trypsin family, histidine proteins from about amino acid 199 to about amino acid 209, from about amino acid 47 to about amino acid 63 and from about amino acid 220 to about amino acid 243 and amino acid sequence blocks having homology to apple domain proteins from about amino acid 222 to about amino acid 249 and from about amino acid 189 to about amino acid 222. Clone DNA65405-1547 has been deposited with ATCC on November 17, 1998 and is assigned ATCC deposit no. 203476.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 102 (SEQ ID NO:170), evidenced significant homology between the PRO1279 amino acid sequence and the following Dayhoff sequences: I56559, S55066, KLK7_RAT, KLK1_RAT, KLKB_RAT, KLK3_MOUSE, KLK8_RAT, AF013988_1, D78203_1 and HSU62801_1.

Additionally, DNA65405-1547 was obtained by purchasing the Incyte EST clone no. 2723646 and sequencing the insert of that clone, thereby giving the DNA65405-1547 sequence shown in Figure 101 (SEQ ID NO:169).

EXAMPLE 55: Isolation of cDNA clones Encoding Human PRO1304

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA35745. Based on the DNA35745 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1304.

PCR primers (forward and reverse) were synthesized:

- forward PCR primer (35745.f1) 5'-GTGTTCTGCTGGAGCCGATGCC-3' (SEQ ID NO:181)
 - forward PCR primer (35745.f2) 5'-GACATGGACAATGACAGG-3' (SEQ ID NO:182)
 - forward PCR primer (35745.f3) 5'-CCTTTCAGGATGTAGGAG-3' (SEQ ID NO:183)
 - 10 forward PCR primer (35745.f4) 5'-GATGTCTGCCACCCCAAG-3' (SEQ ID NO:184)
 - reverse PCR primer (35745.r1) 5'-GCATCCTGATATGACTTGTACGTGGC-3' (SEQ ID NO:185)
 - reverse PCR primer (35745.r2) 5'-TACAAGAGGGAAGAGGAGTTGCAC-3' (SEQ ID NO:186)
- Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35745 sequence which had the following nucleotide sequence
- 15 hybridization probe (35745.p1)
 - 5'-GCCCATATGACGGCTACCTGGCTAAAGACGGCTCGAAATTCTACTGCAGCC-3'(SEQ ID NO:187)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1304 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human ovary tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1304 (designated herein as DNA65406-1567 [Figure 103, SEQ ID NO:179]; and the derived protein sequence for PRO1304.

The entire nucleotide sequence of DNA65406-1567 is shown in Figure 103 (SEQ ID NO:179). Clone DNA65406-1567 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 23-25 and ending at the stop codon at nucleotide positions 689-691 (Figure 103). The predicted polypeptide precursor is 222 amino acids long (Figure 104). The full-length PRO1304 protein shown in Figure 104 has an estimated molecular weight of about 25,794 daltons and a pI of about 6.24. Analysis of the full-length PRO1304 sequence shown in Figure 104 (SEQ ID NO:180) evidences the presence of the following: an endoplasmic reticulum targeting sequence from about amino acid 219 to about amino acid 222, a potential N-glycosylation site from about amino acid 45 to about amino acid 48, FKBP-type peptidyl-prolyl cis-trans isomerase homology blocks from about amino acid 87 to about amino acid 123 and from about amino acid 129 to about amino acid 142 and EF-hand calcium binding domain protein homology blocks from about amino acid 202 to about amino acid 214 and from about amino acid 195 to about amino acid 214. Clone DNA65406-1567 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203219.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 104 (SEQ ID NO:180), evidenced significant

homology between the PRO1304 amino acid sequence and the following Dayhoff sequences: AF040252_1, P_R28980, S71238, CELC05C8_1, VFU52045_1, S75144, FKB3_BOVIN, CELC50F2_6, CELB0511_12 and P_R41781.

The DNA65406-1567 sequence was also obtained by isolating and sequencing the insert of Incyte EST clone no. 2813577.

5

EXAMPLE 56: Isolation of cDNA clones Encoding Human PRO1317

Using the technique described in Example 1 above, Incyte EST no. 33598 was identified as a sequence of interest having a BLAST score of 70 or greater that did not encode a known protein. The sequence of Incyte EST no. 33598 is designated herein as "DNA36958". Based on the DNA36958 sequence, oligonucleotides can be synthesized: 1) to identify by PCR a cDNA library that contains the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1317.

The following are suitable PCR primers (forward and reverse) that can be synthesized based on the DNA36958 sequence:

forward PCR primer: AGGGACCATTGCTTCTTCCAGGCC (36958.f1; SEQ ID NO:190)

15 reverse PCR primer: CGTTACATGTCTCCAAGGGGAATG (36958.r1; SEQ ID NO:191)

Additionally, a synthetic oligonucleotide hybridization probe can be constructed from the consensus DNA36958 sequence having the following nucleotide sequence:

hybridization probe: CCTGTGCTAAGTGCCCCCAAATGCTTCCTGTGTCAATAACACTCACTGC (36958.p1; SEQ ID NO:192)

20 In order to screen several libraries for a source of a full-length clone, DNA from the libraries is screened by PCR amplification with the PCR primer pair identified above. A positive library is then used to isolate clones encoding the PRO1317 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries can be isolated from tissue containing the sequence of interest, for example from peripheral blood, particularly blood taken from a patient having a high leukocyte count (e.g. hypereosinophilia).

The full-length DNA sequence for PRO1317, designated herein as DNA65408-1578 (Figure 105; SEQ ID NO:188) was obtained by purchasing Incyte EST no. 335958, obtaining the cDNA insert, and sequencing it in its entirety. Incyte clone no. 335958 originated from a library constructed using RNA isolated from peripheral blood cells apheresed from a male patient afflicted with hypereosinophilia.

30 The entire coding sequence of PRO1317 is shown in Figure 105 (SEQ ID NO:188). Clone DNA65408-1578 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 6-8 and an apparent stop codon at nucleotide positions 228-230. The predicted polypeptide precursor is 74 amino acids long. The full-length PRO1317 protein shown in Figure 106 has an estimated molecular weight of about 7,831 daltons and a pI of about 9.08. Additional features include: a signal peptide at about amino acids 1-18, potential N-glycosylation sites at about amino acids 34-37 and 39-42, and a microbodies C-terminal targeting signal at amino acids 72-74.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

alignment analysis of the full-length sequence shown in Figure 106 (SEQ ID NO:189), revealed significant homology between the PRO1317 amino acid sequence and the Dayhoff sequence designated CD97_HUMAN. Additionally, some homology was found between the PRO1317 amino acid sequence and the following Dayhoff sequences: GEN12618, CELZK783_1, G156_PARPR, GIAVSPE_1, AF040387_1, S78059, I50617, XLSEK1_1, and NEL2_RAT.

5 Clone DNA65408-1578 was deposited with the ATCC on September 15, 1998, and is assigned ATCC deposit no. 203217.

EXAMPLE 57: Isolation of cDNA clones Encoding Human PRO1303

10 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "DNA47347". Based on the DNA47347 consensus sequence and its homology to an Incyte EST within the assembly from which DNA47347 was derived, Incyte clone 1430305 (from an ileum tissue library) was purchased and sequenced in full. The sequence encoding PRO1303 was thereby identified.

15 The entire coding sequence of PRO1303 is shown in Figure 107 (SEQ ID NO:193). Clone DNA65409-1566 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and an apparent stop codon at nucleotide positions 865-867. The predicted polypeptide precursor is 248 amino acids long. The signal peptide is at about amino acids 1-17 of SEQ ID NO:194. The locations of N-glycosylation sites, active and conserved regions and domains are further indicated in Figure 194. Clone DNA65409-1566 has been deposited with ATCC and is assigned ATCC deposit no. 203232. The full-length
20 PRO1303 protein shown in Figure 108 has an estimated molecular weight of about 26,734 daltons and a pI of about 7.9.

 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 108 (SEQ ID NO:194), revealed sequence identity between the PRO1303 amino acid sequence and the following Dayhoff sequences (data incorporated herein):
25 AB009849_1, P_W08475, AF024605_1, A42048_1, TRY3_RAT, MMAE00066414, TRY1_RAT, MMAE000663_4, MMAE000665_2, and MMAE00066412.

EXAMPLE 58: Isolation of cDNA clones Encoding Human PRO1306

30 Using the method described in Example 1 above, Incyte EST No. 2449282, also referred to herein as DNA5918, was identified as a sequence of interest having a BLAST score of 70 or greater that did not encode a known protein. From the DNA5918 sequence, a consensus sequence was assembled using BLAST and the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is designated herein as "DNA47399". Based on the DNA47399 consensus sequence, oligonucleotides can be synthesized: 1) to identify by PCR a cDNA library that contains the sequence of interest, and 2) for use as
35 probes to isolate a clone of the full-length coding sequence for PRO1306.

 The entire coding sequence of PRO1306 shown in Figure 109 (SEQ ID NO:195), was obtained by purchasing Incyte EST no. 2449282, obtaining the cDNA insert and sequencing it in its entirety. Clone

DNA65410-1569 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 106-108 and an apparent stop codon at nucleotide positions 556-558. The predicted polypeptide precursor is 150 amino acids long. The full-length PRO1306 protein shown in Figure 110 has an estimated molecular weight of about 17,068 daltons, a pI of about 7.29, and a potential N-glycosylation site at about amino acids 131-134.

5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 110 (SEQ ID NO:196), revealed significant homology between the PRO1306 amino acid sequence and Dayhoff sequence AIF1_HUMAN. Homology was also shown between the PRO1306 amino acid sequence and the following Dayhoff sequences: JC4902, BAR1_RAT, AF020281_1, HSU95213_1, TCH3_ARATH, LEY14765_1, CATR_NAEGR, S35185, and
10 AF065247_1.

Clone DNA65410-1569, was deposited with the ATCC on September 15, 1998 and is assigned ATCC deposit no. 203231.

EXAMPLE 59: Isolation of cDNA clones Encoding Human PRO1336

15 An EST sequence was identified and entered into a proprietary Genentech database. The EST was blasted against various EST databases. The EST databases included public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA), and proprietary ESTs from Genentech. The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the ECD protein sequences to a 6 frame
20 translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

A consensus DNA sequence encoding PRO1336 was assembled relative to other aligned EST sequences (forming an assembly) using phrap. This consensus sequence is designated herein "DNA43319". Based on the
25 DNA43319 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1336.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'ATGGAGATTCCTGCCAACTTGCCG3' (SEQ ID NO:199); and
30 reverse PCR primer 5'TTGTGTCATTGAGGAGGAGCAGC3'. (SEQ ID NO:200).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA43319 sequence which had the following nucleotide sequence:

hybridization probe 5'GAGGGCATCGTCGAAATACGCCTAGAACAGAACTCCATCAAAGCCATCCC3'
(SEQ ID NO:201).

35 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1336 gene using the probe oligonucleotide and one of the PCR primers. RNA

for construction of the cDNA libraries was isolated from human fetal lung tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1336 (designated herein as DNA65423-1595 [Figures 111A-B, SEQ ID NO:198]; and the derived protein sequence for PRO1336.

The entire coding sequence of PRO1336 is shown in Figures 111A-B (SEQ ID NO:198). Clone
5 DNA65423-1595 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 83-85 and an apparent stop codon at nucleotide positions 4652-4654 of SEQ ID NO:198. The predicted polypeptide precursor is 1523 amino acids long. The approximate locations of the signal peptide (amino acids 1-27), aspartic acid and asparagine hydroxylation sites, EGF-like domain cystein pattern signature regions, a leucine zipper pattern region, a region conserved in immunoglobulins and major histocompatibility complexes,
10 and N-glycosylation sites are indicated in Figure 112. Clone DNA65423-1595 has been deposited with the ATCC and is assigned ATCC deposit no. 203227. The full-length PRO1336 protein shown in Figure 112 has an estimated molecular weight of about 167,715 daltons and a pI of about 8.06.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 112 (SEQ ID NO:198), revealed sequence identity
15 between the PRO1336 amino acid sequence and the following Dayhoff sequences (data incorporated herein): SLIT_DROME, CEF40E10_1, LCU58977_1, AF029779_1, FBP1_STRPU, NOTC_XENLA, AC004663_1, XELXDEL_1, P_W05835 and HSU77720_1.

EXAMPLE 60: Isolation of cDNA clones Encoding Human PRO1278

20 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "Consen5230". In addition, the Consen5230 consensus sequence was extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is designated herein as "DNA44801". Based on the DNA44801 consensus sequence, oligonucleotides were
25 synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1278.

PCR primers (forward and reverse) were synthesized:

forward PCR primers: GCAGGCTTTGAGGATGAAGGCTGC (44801.f1; SEQ ID NO:204) and CTCATTGGCTGCCTGGTCACAGGC (44801.f2; SEQ ID NO:205)

30 reverse PCR primers: CCAGTCGGACAGGTCTCTCCCCTC (44801.r1; SEQ ID NO:206) and TCAGTGACCAAGGCTGAGCAGGCG (44801.r2; SEQ ID NO:207)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA44801 sequence which had the following nucleotide sequence:

hybridization probe: CTACACTCGTTGCAAACCTGGCAAAAATATTCTCGAGGGCTGGCCTGG44801.p1;
35 SEQ ID NO:208)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to

isolate clones encoding the PRO1278 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human testis.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1278 (designated herein as DNA66304-1546 [Figure 113, SEQ ID NO:202]; and the derived protein sequence for PRO1278.

5 The entire coding sequence of PRO1278 is shown in Figure 113 (SEQ ID NO:202). Clone DNA66304-1546 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 141-143 and an apparent stop codon at nucleotide positions 585-587. The predicted polypeptide precursor is 148 amino acids long. The full-length PRO1278 protein shown in Figure 114 has an estimated molecular weight of about 16,623 daltons and a pI of about 8.47. Additional features include a signal peptide sequence at about
10 amino acids 1-19; a potential N-glycosylation site at about amino acids 58-61; an alpha-lactalbumin/lysozyme C signature at about amino acids 94-112; and homolgy with alpha-lactalbumin/lysozyme C at about amino acids 35-59, 67-59 and 112-133.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 114 (SEQ ID NO:203), revealed significant
15 homology between the PRO1278 amino acid sequence and the following Dayhoff sequences: LYC1_ANAPL, LYC3_ANAPL, and LYC_HUMAN.

Clone DNA66304-1546 was deposited with the ATCC on October 6, 1998, and is assigned ATCC deposit no. 203321.

20 EXAMPLE 61: Isolation of cDNA clones Encoding Human PRO1298

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from an Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One
25 or more of the ESTs was derived from a diseased prostate tissue library. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein
30 designated DNA56389.

In light of the sequence homology between the DNA56389 sequence and an EST sequence contained within an Incyte EST within the assembly from with the consensus sequence was derived, Incyte clone 3355717 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 115 and is herein designated as DNA66511-1563.

35 The full length clone shown in Figure 115 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 94-96 and ending at the stop codon found at nucleotide positions 1063-1065 (Figure 115; SEQ ID NO:209). The predicted polypeptide precursor (Figure 116, SEQ ID NO:210)

is 323 amino acids long. The signal peptide is at about amino acids 1-15 of SEQ ID NO:210. PRO1298 has a calculated molecular weight of approximately 37,017 daltons and an estimated pI of approximately 8.83. Clone DNA66511-1563 was deposited with the ATCC on September 15, 1998 and is assigned ATCC deposit no. 203228.

5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 116 (SEQ ID NO:210), revealed sequence identity between the PRO1298 amino acid sequence and the following Dayhoff sequences (data incorporated herein): ALG2_YEAST, CAPM_STAAU, C69098, C69255, SUS2_MAIZE, A69143, S74778, AB009527_13, AF050103_2 and BBA224769_1.

10 EXAMPLE 62: Isolation of cDNA clones Encoding Human PRO1301

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte Cluster No. 93492, also referred herein as "DNA10591". This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database
15 (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs was derived from a
20 cDNA library constructed from RNA isolated from lung tissue removed from a male with adenocarcinoma. The consensus sequence obtained therefrom is herein designated "DNA57725".

In light of the sequence homology between the DNA57725 sequence and an EST sequence contained within the EST no. 3395984, the EST clone 3395984 was purchased and the cDNA insert was obtained and sequenced in its entirety. The sequence of this cDNA insert is shown in Figure 117 and is herein designated as
25 "DNA66512-1564".

The full length clone shown in Figure 117 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 43 to 45 and ending at the stop codon found at nucleotide positions 1429 to 1431 (Figure 117; SEQ ID NO:211). The predicted polypeptide precursor (Figure 118, SEQ ID NO:212) is 462 amino acids long. Other features of the PRO1301 protein include: a signal sequence at about
30 amino acids 1-18; a transmembrane domain at about amino acids 271-290; a cytochrome P450 homologous region at about amino acids 134-462; and potential N-glycosylation sites at about amino acids 94-97, 217-220, and 246-249. PRO1301 has a calculated molecular weight of approximately 52,432 daltons and an estimated pI of approximately 6.14. Clone DNA66512-1564 was deposited with the ATCC on September 15, 1998 and is assigned ATCC deposit no. 203218.

35 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 118 (SEQ ID NO:212), revealed some homology between the PRO1301 amino acid sequence and the following Dayhoff sequences: PSU29243_1, A69975,

ATAC00448418, D78607_1, CEB0331_1, HUMCYTHIA_1, AF014800_1, CELT13C5_4, CELC45H4_14, and CEC54E10_1.

EXAMPLE 63: Isolation of cDNA clones Encoding Human PRO1268

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated EST No. 8879. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs was derived from a cDNA library constructed from human brain tumor tissue taken from a cerebral meninges lesion. The consensus sequence obtained therefrom is herein designated DNA56258.

In light of the sequence homology between the DNA56258 sequence and an EST sequence contained within the Incyte EST no. 2944541, EST clone no. 2944541 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 119 and is herein designated as "DNA66519-1535".

The full length clone shown in Figure 119 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 89 to 91 and ending at the stop codon found at nucleotide positions 509 to 511 (Figure 119; SEQ ID NO:213). The predicted polypeptide precursor (Figure 120, SEQ ID NO:214) is 140 amino acids long. PRO1268 has a calculated molecular weight of approximately 15,503 daltons and an estimated pI of approximately 6.44. Additional features include a type II transmembrane domain at about amino acids 12-28; type I transmembrane domains at about amino acids 51-66 and 107-124; a potential N-glycosylation site at about amino acids 79-82, and a region having homology with G-protein coupled receptors at about amino acids 59-99.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 120 (SEQ ID NO:214), revealed some homology between the PRO1268 amino acid sequence and Dayhoff sequence no. CEF39B2_9. However, the percent sequence identity was determined to not be significant.

Clone DNA66519-1535 was deposited with the ATCC on September 15, 1998 and is assigned ATCC deposit no. 203236.

EXAMPLE 64: Isolation of cDNA clones Encoding Human PRO1269

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated EST Cluster No. 101920. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases

(e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56509.

In light of the sequence homology between the DNA56509 sequence and an EST sequence contained within the EST no. 103157, EST clone no.103157 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 121 and is herein designated as DNA66520-1536.

The full length clone shown in Figure 121 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 26-29 and ending at the stop codon found at nucleotide positions 614-616 (Figure 121; SEQ ID NO:215). The predicted polypeptide precursor (Figure 122, SEQ ID NO:216) is 196 amino acids long, with a signal peptide located at about amino acids 1-20. There is a potential N-glycosylation site at about amino acids 112-115. PRO1269 has a calculated molecular weight of approximately 21,731 daltons and an estimated pI of approximately 8.97.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 122 (SEQ ID NO:216), revealed significant homology between the PRO1269 amino acid sequence and the amino acid sequence of Dayhoff sequence no. P_W23722. In addition, sequence homology was found between the PRO1269 amino acid sequences and the amino acid sequences of the following Dayhoff sequences: MMTAG7_1, MTV026_16, NAAA_BPT3, S75616_1, and NCP_PIG.

Clone DNA66520-1536 was deposited with the ATCC on September 15, 1998, and is assigned ATCC deposit no. 203226.

EXAMPLE 65: Isolation of cDNA clones Encoding Human PRO1327

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 173410. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56520.

In light of the sequence homology between the DNA56520 sequence and an EST sequence contained within the Incyte EST clone no. 3451760, the Incyte EST clone no. 3451760 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 123 and is herein designated

as DNA66521-1583.

Clone DNA66521-1583 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 55-57 and ending at the stop codon at nucleotide positions 811-813 (Figure 123). The predicted polypeptide precursor is 252 amino acids long (Figure 124). The full-length PRO1327 protein shown in Figure 124 has an estimated molecular weight of about 28,127 daltons and a pI of about 8.91. Analysis of the full-length PRO1327 sequence shown in Figure 124 (SEQ ID NO:218) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 14, potential N-glycosylation sites from about amino acid 62 to about amino acid 65, from about amino acid 127 to about amino acid 130, from about amino acid 137 to about amino acid 140 and from about amino acid 143 to about amino acid 146 and a 2-oxo acid dehydrogenase acyltransferase homology block from about amino acid 61 to about amino acid 71. Clone DNA66521-1583 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203225.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 124 (SEQ ID NO:218), evidenced significant homology between the PRO1327 amino acid sequence and the following Dayhoff sequences: NPH1_RAT, NPH2_MOUSE, OTU_DROME, D40750, BB61_RABIT, P_R23873, P_W09643, CAGHMGPA_1, HUMPRP11_1 and S670958_1.

EXAMPLE 66: Isolation of cDNA clones Encoding Human PRO1382

Using the method described in Example 1 above, Incyte EST no. 2719 was identified as a sequence of interest having a BLAST score of 70 or greater that does not encode a known protein. The nucleotide sequence of EST no. 2719 is designated herein "DNA42842". Based on the DNA42842 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1382.

PCR primers (forward and reverse) were synthesized:

forward PCR primer ACGGCTCACCATGGGCTCCG (42842.f1; SEQ ID NO:221)

reverse PCR primer AGGAAGAGGAGCCCTTGGAGTCCG (42842.r1; SEQ ID NO:222)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA42842 sequence which had the following nucleotide sequence:

hybridization probe CGTGCTGGAGGGCAAGTGTCTGGTGGTGTGCGACTCGAAC (42842.p1; SEQ ID NO:223).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1382 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from a human breast carcinoma.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1382 (designated herein as DNA66526-1616 [Figure 125, SEQ ID NO:219]; and the derived protein sequence for PRO1382.

The entire coding sequence of PRO1382 is shown in Figure 125 (SEQ ID NO:219). Clone DNA66526-1616 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 337-339 and an apparent stop codon at nucleotide positions 940-942. The predicted polypeptide precursor is 201 amino acids long. The full-length PRO1382 protein shown in Figure 126 has an estimated molecular weight of about 21,808 daltons and a pI of about 9.04. Additional features include a signal peptide at about amino acids 1-27; potential N-glycosylation sites at about amino acids 29-32 and 88-91; and regions of homology with C1q proteins at about amino acids 92-126, 159-178, and 191-200.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 126 (SEQ ID NO:220), revealed significant homology between the PRO1382 amino acid sequence Dayhoff sequence no. CERL_RAT. Homology was also revealed between the PRO1382 amino acid sequence and the following Dayhoff sequences: CERB_HUMAN, S76975_1, A41752, HUMC1QB2_1, A57131, CA1A_HUMAN, ACR3_MOUSE, and COLE_LEPMA.

Clone DNA66526-1616 has been deposited with ATCC and is assigned ATCC deposit no. 203246.

EXAMPLE 67: Isolation of cDNA clones Encoding Human PRO1328

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 40671. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56749.

In light of the sequence homology between the DNA56749 sequence and an EST sequence contained within the Incyte EST clone no. 4111192, the Incyte EST clone no. 4111192 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 127 and is herein designated as DNA66658-1584.

Clone DNA66658-1584 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 9-11 and ending at the stop codon at nucleotide positions 780-782 (Figure 127). The predicted polypeptide precursor is 257 amino acids long (Figure 128). The full-length PRO1328 protein shown in Figure 128 has an estimated molecular weight of about 28,472 daltons and a pI of about 9.33. Analysis of the full-length PRO1328 sequence shown in Figure 128 (SEQ ID NO:225) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, transmembrane domains from about amino acid 32 to about amino acid 51, from about amino acid 119 to about amino acid 138, from about amino acid 152 to about amino acid 169 and from about amino acid 216 to about amino acid 235, a glycosaminoglycan attachment site from about amino acid 120 to about amino acid 123 and sodium/neurotransmitter symporter family protein homology block from about amino acid 31 to about amino acid 65. Clone DNA66658-1584 has

been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203229.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 128 (SEQ ID NO:225), evidenced significant homology between the PRO1328 amino acid sequence and the following Dayhoff sequences: CEVF36H2L_2, TIP2_TOBAC, AB009466_16, ATU39485_1, P_R60153, P_R77082, S73351, C69392, LEU95008_1 and E64667.

EXAMPLE 68: Isolation of cDNA clones Encoding Human PRO1325

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 139524. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56115.

In light of the sequence homology between the DNA56115 sequence and an EST sequence contained within the Incyte EST clone no. 3744079, the Incyte EST clone no. 3744079 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 129 and is herein designated as DNA66659-1593.

Clone DNA66659-1593 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 51-53 and ending at the stop codon at nucleotide positions 2547-2549 (Figure 129). The predicted polypeptide precursor is 832 amino acids long (Figure 130). The full-length PRO1325 protein shown in Figure 130 has an estimated molecular weight of about 94,454 daltons and a pI of about 6.94. Analysis of the full-length PRO1325 sequence shown in Figure 130 (SEQ ID NO:227) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 18, transmembrane domains from about amino acid 292 to about amino acid 317, from about amino acid 451 to about amino acid 470, from about amino acid 501 to about amino acid 520, from about amino acid 607 to about amino acid 627 from about amino acid 751 to about amino acid 770, a leucine zipper pattern sequence from about amino acid 497 to about amino acid 518 and potential N-glycosylation sites from about amino acid 27 to about amino acid 30, from about amino acid 54 to about amino acid 57, from about amino acid 60 to about amino acid 63, from about amino acid position 123 to about amino acid position 126, from about amino acid position 141 to about amino acid position 144, from about amino acid position 165 to about amino acid position 168, from about amino acid position 364 to about amino acid position 367, from about amino acid position 476 to about amino acid position 479, from about amino acid position 496 to about amino acid position 499, from about amino acid position 572 to about amino acid position 575, from about amino acid position 603 to about amino acid position 606 and from about amino acid position 699 to about amino acid position 702. Clone DNA66659-1593 has been deposited with ATCC on

September 22, 1998 and is assigned ATCC deposit no. 203269.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 130 (SEQ ID NO:227), evidenced significant homology between the PRO1325 amino acid sequence and the following Dayhoff sequences: CELR04E5_1, CELZK721_5, CELC30E1_5, CELC30E1_6, CELC30E1_2, CEY37H2C_1, CELC30E1_7, CELT07H8_7 and
5 E64006.

EXAMPLE 69: Isolation of cDNA clones Encoding Human PRO1340

Using the method set forth in Example 1 above, Incyte EST no. 878906 was identified as a sequence of interest having a BLAST score of 70 or greater that does not encode a known protein. The nucleotide
10 sequence of EST no. 878906 is designated herein "DNA42809". Based on the DNA42809 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1340.

PCR primers (forward and reverse) were synthesized:

forward PCR primer TCCAGGTGGACCCCACTTCAGG (42809.f1; SEQ ID NO:270)

15 reverse PCR primer GGGAGGCTTATAGGCCCAATCTGG (42809.r1; SEQ ID NO:271)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA42809 sequence which had the following nucleotide sequence:

hybridization probe GGCTTCAGCAGCACGTGTGAAGTCGAAGTCGCAGTCACAGATATCAATGA
(42809.p1; SEQ ID NO:272)

20 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1340 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for
25 PRO1340 (designated herein as DNA66663-1598 [Figure 131, SEQ ID NO:228]; and the derived protein sequence for PRO1340.

The entire coding sequence of PRO1340 is shown in Figure 131 (SEQ ID NO:228). Clone DNA66663-1598 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 128-130 and an apparent stop codon at nucleotide positions 2549-2551. The predicted polypeptide precursor
30 is 807 amino acids long. The full-length PRO1340 protein shown in Figure 132 has an estimated molecular weight of about 87,614 daltons and a pI of about 4.83. Additional features include: a signal peptide at about amino acids 1-18; a transmembrane domain at about amino acids 762-784; a cell attachment sequence at about amino acids 492-494; potential N-glycosylation sites at about amino acids 517-520, 602-605 and 700-703; and cadherin extracellular repeat domains at about amino acids 307-351, 324-348, 67-103, 97-141 and 114-138.

35 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 132 (SEQ ID NO:229), revealed significant homology between the PRO1340 amino acid sequence and Dayhoff sequence no. I46536. Homology was also

revealed between the PRO1340 amino acid sequence and the following Dayhoff sequences: S55396, RATPDRPT_1, CADD_CHICK, CAD1_CHICK, CADB_CHICK, I50180, CAD4_CHICK, G02878, and DSC1_MOUSE.

Clone DNA66663-1598 has been deposited with ATCC and is assigned ATCC deposit no. 203268.

5 EXAMPLE 70: Isolation of cDNA clones Encoding Human PRO1339

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "DNA40652". Within the consensus sequence assembly was Incyte EST 2479394. Based on the consensus sequence and other discoveries and information provided herein, the clone including Incyte EST 2479394 was purchased and sequenced in full.

10 Sequencing provided the nucleic acid sequence shown in Figure 133 which includes the sequence encoding PRO1339.

Clone DNA66669-1597 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 9-11 and an apparent stop codon at nucleotide positions 1272-1274 of SEQ ID NO:233. The predicted polypeptide precursor is 421 amino acids long. The signal peptide is at about amino acids 1-16 of SEQ ID NO:234. The region conserved in zinc carboxypeptidases and the N-glycosylation site are indicated in Figure 134. Clone DNA66669-1597 has been deposited with the ATCC and is assigned ATCC deposit no. 203272. The full-length PRO1339 protein shown in Figure 134 has an estimated molecular weight of about 47,351 daltons and a pI of about 6.61.

20 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 134 (SEQ ID NO:234), revealed sequence identity between the PRO1339 amino acid sequence and the following Dayhoff sequences (data incorporated herein): P_W01505, CBP1_HUMAN, HSA224866_1, P_R90293, YHT2_YEAST, CEF02D8_4, CEW01A8_6, P_W36815, HSU83411_1 and CBPN_HUMAN.

25 EXAMPLE 71: Isolation of cDNA clones Encoding Human PRO1337

Using the method described in Example 1 above, a single Incyte EST was identified (EST No.1747546) and also referred to herein as "DNA4417". To assemble a consensus sequence, repeated cycles of BLAST and phrap were used to extend the DNA4417 sequence as far as possible using the sources of EST sequences discussed above. The consensus sequence is designated herein as "DNA45669". Based on the DNA45669 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1337.

PCR primers (forward and reverse) were synthesized:

35 forward PCR primers: CAACCATGCAAGGACAGGGCAGG (45669.f1; SEQ ID NO:237) and CTTTGCTGTTGGCCTCTGTGCTCCCAACCATGCAAGGACAGGGCAGG (45669.r1; SEQ ID NO:238);
reverse PCR primers: TGACTCGGGGTCTCCAAAACCAGC (45669.r1; SEQ ID NO:239) and GGTATAGGCGGAAGGCAAAGTCGG (45669.r2; SEQ ID NO:240);

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45669 sequence which had the following nucleotide sequence:

hybridizationprobe: GGCATCTTACCTTTATGGAGTACTCTTTGCTGTTGGCCTCTGTGCTCC(45669.pl; SEQ ID NO:241).

5 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1337 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1337 (designated herein as DNA66672-1586 [Figure 135, SEQ ID NO:235]; and the derived protein
10 sequence for PRO1337.

The entire coding sequence of PRO1337 is shown in Figure 135 (SEQ ID NO:235). Clone DNA66672-1586 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 60-62 and an apparent stop codon at nucleotide positions 1311-1313. The predicted polypeptide precursor is 417 amino acids long. The full-length PRO1337 protein shown in Figure 136 has an estimated molecular weight of
15 about 46,493 daltons and a pI of about 9.79.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 136 (SEQ ID NO:236) revealed significant homology between the PRO1337 amino acid sequence and the Dayhoff sequence THBG_HUMAN. Homology was also found between the PRO1337 amino acid sequence and the following Dayhoff sequences:
20 KAIN_HUMAN, HSACT1_1, IPSP_HUMAN, G02081, HAMHPP_1, CPI6_RAT, S31507, AB000547_1, and KBP_MOUSE.

Clone DNA66672-1586 was deposited with the ATCC on September 22, 1998, and is assigned ATCC deposit no. 203265.

25 EXAMPLE 72: Isolation of cDNA clones Encoding Human PRO1342

A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated DNA43203. The DNA43203 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and proprietary EST DNA databases (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA; Genentech, South San Francisco, CA) to identify
30 existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is designated herein as "DNA48360".

35 Based on the DNA48360 sequence, oligonucleotide probes were generated and used to screen a human esophageal tissue library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science,

253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-GAAGCACCAGCCTTTATCTCTTCACC-3' (48360.f1; SEQ ID NO:244)

reverse PCR primer: 5'-GTCAGAGTTGGTGGCTGTGCTAGC-3' (48360.r1; SEQ ID NO:245)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA48360 sequence

5 which had the following nucleotide sequence:

hybridization probe:

5'GGACCCAGGCATCTTGCTTTCCAGCCACAAAGAGACAGATGAAGATGC-3 (48360.p1; SEQ ID NO:246)

10 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1342 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 239-241, and a stop signal at nucleotide positions 2027-2029 (Figure 137; SEQ ID NO:242). The predicted polypeptide precursor is 596 amino acids long has a calculated
15 molecular weight of approximately 57,173 daltons and an estimated pI of approximately 4.82. Additional features include: signal sequence at about amino acids 1-20; a transmembrane domain at about amino acids 510-532; a potential N-glycosylation site at about amino acids 25-28; a glycosaminoglycan attachment site at about amino acids 325-328; and bacterial ice-nucleation protein octamer repeats at about amino acids 284-337, 404-457, 254-307, 359-412, 194-247, 239-292, 299-352, 134-187, 314-367, and 164-217.

20 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 138 (SEQ ID NO:243), evidenced some homology between the PRO1342 amino acid sequence and the following Dayhoff sequences: CELZC178_2, LMSAP2GN_1, D88734_, AMYH_YEAST, MMDSPPG_1, VGLX_HSVEB, S52714, CELF59A6_5, CELK06A9_3, and YM96_YEAST.

25 Clone DNA66674-1599 was deposited with the ATCC on September 22, 1998, and is assigned ATCC deposit no. 203281.

EXAMPLE 73: Isolation of cDNA clones Encoding Human PRO1343

A cDNA sequence isolated in the amylase screen described in Example 2 above was found, by the WU-
30 BLAST2 sequence alignment computer program, to have no significant sequence identity to any known human encoding nucleic acid. This cDNA sequence is herein designated DNA48921. Probes were generated from the sequence of the DNA48921 molecule and used to screen a human smooth muscle cell tissue library prepared as described in paragraph 1 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less
35 than 2800 bp.

The oligonucleotide probes employed were as follows:

forward PCR primer (48921.f1) 5'-CAATATGCATCTTGACGCTCTGG-3' (SEQ ID NO:249)

reverse PCR primer (48921.r1) 5'-AAGCTTCTCTGCTTCCTTTCCTGC-3' (SEQ ID NO:250)

hybridization probe (48921.p1)

5'-TGACCCCATGAGAAGGTCATTGAAGGGATCAACCGAGGGCTG-3' (SEQ ID NO:251)

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 71-73 and a stop signal at nucleotide positions 812-814 (Figure 139, SEQ ID NO:247). The predicted polypeptide precursor is 247 amino acids long, has a calculated molecular weight of approximately 25,335 daltons and an estimated pI of approximately 7.0. Analysis of the full-length PRO1343 sequence shown in Figure 140 (SEQ ID NO:248) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25 and a homologous region to circumsporozoite repeats from about amino acid 35 to about amino acid 225. Clone DNA66675-1587 has been deposited with ATCC on September 22, 1998 and is assigned ATCC deposit no. 203282.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 140 (SEQ ID NO:248), evidenced significant homology between the PRO1343 amino acid sequence and the following Dayhoff sequences: CSP_PLACC, CEF25H8_2, U88974_40, BNAMRNAA_1, BOBOPC3_1, S58135, AF061832_1, BHU52040_1, HUMPROFILE_1 and MTV023_14.

Additionally, an Incyte EST clone (Incyte EST clone no. 4701148) having homology to the DNA48921 sequence was obtained and the insert sequenced, thereby giving rise to the DNA66675-1587 sequence shown in Figure 139.

EXAMPLE 74: Isolation of cDNA clones Encoding Human PRO1480

Using the methods described in Example 1 above, Incyte EST Nos. 550415 and 1628847 were identified as sequences of interest having BLAST scores of 70 or greater that did not encode known proteins. These sequences were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is designated herein as "DNA1395". In addition, the "DNA1395" consensus sequence was extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is designated herein as "DNA40642". Based on the DNA40642 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1480.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: AGCCCGTGCAGAATCTGCTCCTGG (40642.f1; SEQ ID NO:254)

reverse PCR primers: TGAAGCCAGGGCAGCGTCCTCTGG (40642.r1; SEQ ID NO:255);
GTACAGGCTGCAGTTGGC (40642.r2; SEQ ID NO:256)

Additionally, synthetic oligonucleotide hybridization probes were constructed from the consensus DNA40642 sequence which had the following nucleotide sequence:

hybridization probes: AGAAGCCATGTGAGCAAGTCCAGTTCCAGCCCAACACAGTG(40642.p1; SEQ ID NO:257); GAGCTGCAGATCTTCTCATCGGGACAGCCCGTGCAGAATCTGCTC (40642.p2; SEQ ID

NO:258).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1480 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

5 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1480, designated herein as DNA67962-1649 [Figure 141, SEQ ID NO:252]; and the derived protein sequence for PRO1480.

The entire coding sequence of PRO1480 is shown in Figure 141 (SEQ ID NO:252). Clone DNA67962-1649 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 241-243 and an apparent stop codon at nucleotide positions 2752-2754. The predicted polypeptide precursor is 837 amino acids long. The full-length PRO1480 protein shown in Figure 142 has an estimated molecular weight of about 92,750 daltons and a pI of about 7.04. Additional features include: transmembrane domains at about amino acids 23-46 (type II) and 718-738; potential N-glycosylation sites at about amino acids 69-72, 96-99, 165-168, 410-413, 525-528, and 630-633; and a leucine zipper pattern at about amino acids 12-33.

15 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 142 (SEQ ID NO:253), revealed significant homology between the PRO1480 amino acid sequence and Dayhoff sequence I48746. Homology was also shown between the PRO1480 amino acid sequence and the following Dayhoff sequences: S66498; P_W17658; MMU69535_1; HSU60800_1; I48745; A49069; I48747; GGU28240_1; and AF022946_1.

20 Clone DNA67962-1649 has been deposited with ATCC and is assigned ATCC deposit no. 203291.

EXAMPLE 75: Isolation of cDNA clones Encoding Human PRO1487

A single Merck EST, HSC2ID011, referred herein as "DNA8208", was identified as an EST of interest having a BLAST score of 70 or greater that did not encode a known protein as described in Example 1 above. The DNA8208 sequence was extended using repeated cycles of BLAST and the program "phrap" (Phil Green, University of Washington, Seattle, Washington) to extend the sequence as far as possible using the sources of EST sequences discussed above. The resulting consensus sequence is designated herein as "DNA68836". Based on the DNA68836 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1487.

30 PCR primers (forward and reverse) were synthesized:

forward PCR primer: GTGCCACTACGGGGTGTGGACGAC (54209.f1; SEQ ID NO:261) and

reverse PCR primer: TCCCATTTCTTCCGTGGTGCCAG (54209.r1; SEQ ID NO:262)

35 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA68836 sequence which had the following nucleotide sequence:

hybridization probe: CCAGAAGAAGTCCTTCATGATGCTCAAGTACATGCACGACCACTAC (54209.p1; SEQ ID NO:263)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1487 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated human fetal kidney tissue.

5 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1487 (designated herein as DNA68836-1656 (Figures 143A-B; SEQ ID NO:259) and the derived protein sequence for PRO1487 (Figure 144; SEQ ID NO:260).

The entire coding sequence of PRO1487 is shown in Figures 143A-B (SEQ ID NO:259). Clone DNA68836-1656 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 489-491 and an apparent stop codon at nucleotide positions 2895-2897. The predicted polypeptide precursor is 802 amino acids long. The full-length PRO1487 protein shown in Figure 144 has an estimated molecular weight of about 91,812 daltons and a pI of about 9.52. Additional features include a signal peptide at about amino acids 1-23; potential N-glycosylation sites at about amino acids 189-192, 623-626, and 796-799; and a cell attachment sequence at about amino acids 62-64.

15 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 144 (SEQ ID NO:260), revealed significant homology between the PRO1487 amino acid sequence and the following Dayhoff sequences: CET24D1_1, S44860, CELC02H6_1, CEC38H2_3, CELC17A2_5, CET09E11_10, CEE03H4_3, CELT22B11_3, GGU82088_1, and CEF56H6_1.

20 Clone DNA68836-1656 was deposited with the ATCC on November 3, 1998, and is assigned ATCC deposit no. 203455.

EXAMPLE 76: Isolation of cDNA clones Encoding Human PRO1418

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from an Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from a placenta tissue library. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA58845.

35 In light of the sequence homology between the DNA58845 sequence and an EST included in Incyte clone 1306026, that clone was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 145 and is herein designated as DNA68864-1629.

The full length clone shown in Figure 145 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 138-140 and ending at the stop codon found at nucleotide

positions 1188-1190 (Figure 145; SEQ ID NO:264). The predicted polypeptide precursor (Figure 146, SEQ ID NO:265) is 350 amino acids long with a signal peptide at about amino acids 1-19 of SEQ ID NO:265. PRO1418 has a calculated molecular weight of approximately 39,003 daltons and an estimated pI of approximately 5.59. Clone DNA68864-1629 was deposited with the ATCC on September 22, 1998 and is assigned ATCC deposit no. 203276.

- 5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 146 (SEQ ID NO:265), revealed sequence identity between the PRO1418 amino acid sequence and the following Dayhoff sequences (data incorporated herein): AGA1_HAEIN (immunoglobulin a1 protease precursor), P_W03740, CELT23E7_1, SSN6_YEAST, MMPININ_1, AB00993_1, P_R52601, S22624, A10377_1 and MUA1_XENLA.

10

EXAMPLE 77: Isolation of cDNA clones Encoding Human PRO1472

- An Incyte sequence was identified and put in a computer to determine whether it had homology with other proteins in databases. The EST databases included public EST databases (e.g., GenBank), and the proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

- 20 A consensus DNA sequence encoding PRO1472 was assembled relative to other EST sequences using phrap. This consensus sequence is designated herein "DNA62824". Based on the DNA62824 consensus sequence and other discoveries and information provided herein, the Incyte clone including EST 1579843 (from a duodenal tissue library) found in the assembly was purchased and sequenced in full.

- 25 Sequencing provided the entire coding sequence of PRO1472 as shown in Figure 147 (SEQ ID NO:266). Clone DNA68866-1644 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 134-136 and an apparent stop codon at nucleotide positions 1532-1534 of SEQ ID NO:266. The predicted polypeptide precursor is 466 amino acids long. As indicated in Figure 148, the signal peptide is at about amino acid positions 1-17 and the transmembrane domains are at about positions 131-150 and 235-259 of SEQ ID NO:267. Clone DNA68866-1644 has been deposited with ATCC and is assigned ATCC deposit no. 203283. The full-length PRO1472 protein shown in Figure 148 has an estimated molecular weight of about 52,279 daltons and a pI of about 6.16.

- 30 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 148 (SEQ ID NO:267), revealed sequence identity between the PRO1472 amino acid sequence and the following Dayhoff sequences (data incorporated herein): BUTY_HUMAN, HS45P21_1, HS45P21_3, HS45P21_5, HS45P21_4, HSU90142_1, HSU90546_1, AF033107_1, MMHC135G15_7 and HSB73_1.

EXAMPLE 78: Isolation of cDNA clones Encoding Human PRO1461

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte EST Cluster No. 159103, and also referred to herein as "DNA10747". The DNA10747 sequence was then compared to a variety of EST databases which included public EST databases (e.g., GenBank) and the LIFESEQ® database, to identify existing homologies.

5 The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs used in the assembly was derived from a library constructed from pancreatic tumor tissue. The consensus

10 sequence obtained therefrom is herein designated "DNA59553".

In light of the sequence homology between the DNA59553 sequence and an EST sequence contained within Incyte EST no. 2944541, the EST clone was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 149 and is herein designated as DNA68871-1638.

The full length clone shown in Figure 149 contained a single open reading frame with an apparent

15 translational initiation site at nucleotide positions 32-34 and ending at the stop codon found at nucleotide positions 1301-1303 (Figure 149; SEQ ID NO:268). The predicted polypeptide precursor (Figure 150, SEQ ID NO:269) is 423 amino acids long. PRO1461 has a calculated molecular weight of approximately 47,696 daltons and an estimated pI of approximately 8.96. Additional features include: a type II transmembrane domain at about amino acids 21-40; an ATP/GTP-binding site motif A (P-loop) at about amino acids 359-366; a trypsin family histidine

20 active site at about amino acids 228-233; potential N-myristoylation sites at about amino acids 179-184, 213-218, 317-322, and 360-365; and potential N-glycosylation sites at about amino acids 75-78, 166-169 and 223-226.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 150 (SEQ ID NO:269), revealed significant homology between the PRO1461 amino acid sequence Dayhoff sequence no. P_R89435. Homology was also

25 found to exist between the PRO1461 amino acid sequence and the following additional Dayhoff sequences: AB002134_1, P_R89430, P_W22987, HEPS_MOUSE, ENTK_HUMAN, P_W22986, KAL_MOUSE, ACRO_PIG, p_R57283, and TRY7_ANOGA.

Clone DNA68871-68871 was deposited with the ATCC on September 22, 1998, and is assigned ATCC deposit no.203280.

30

EXAMPLE 79: Isolation of cDNA clones Encoding Human PRO1410

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 98502. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST

35 databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a

BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56451.

5 In light of the sequence homology between the DNA56451 sequence and an EST sequence contained within the Incyte EST clone no. 1257046, the Incyte EST clone 125046 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 151 and is herein designated as DNA68874-1622.

10 Clone DNA68874-1622 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 152-154 and ending at the stop codon at nucleotide positions 866-868 (Figure 151). The predicted polypeptide precursor is 238 amino acids long (Figure 152). The full-length PRO1410 protein shown in Figure 152 has an estimated molecular weight of about 25,262 daltons and a pI of about 6.44. Analysis of the full-length PRO1410 sequence shown in Figure 152 (SEQ ID NO:271) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 20, a transmembrane domain from about amino acid 194 to about amino acid 220 and a potential N-glycosylation site from about amino acid 132 to about amino acid 135. Clone DNA68874-1622 has been deposited with ATCC on September 22, 1998 and is assigned
15 ATCC deposit no. 203277

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 152 (SEQ ID NO:271), evidenced significant homology between the PRO1410 amino acid sequence and the following Dayhoff sequences: I48652, P_R76466, HSMHC3W36A_2, EPB4_HUMAN, P_R14256, EPA8_MOUSE, P_R77285, P_W13569, AF000560_1, and
20 ASF1_HELAN.

EXAMPLE 80: Isolation of cDNA clones Encoding Human PRO1568

A consensus DNA sequence was assembled relative to other EST sequences using phrap to form an assembly as described in Example 1 above. The consensus sequence is designated herein "DNA54208". Based
25 on the DNA54208 consensus sequence, the assembly and other information and discoveries provided herein, a clone including an EST in the assembly was ordered and sequenced. The EST is Incyte 3089490. Sequencing in full gave the sequence shown in Figure 153.

The entire coding sequence of PRO1568 is included in Figure 153 (SEQ ID NO:272). Clone DNA68880-1676 contains a single open reading frame with an apparent translational initiation site at nucleotide
30 positions 208-210 and an apparent stop codon at nucleotide positions 1123-1125 of SEQ ID NO:272. The predicted polypeptide precursor is 305 amino acids long. The signal peptide, transmembrane regions, N-myristoylation and amidation sites are also indicated in Figure 154. Clone DNA68880-1676 has been deposited with the ATCC and is assigned ATCC deposit no. 203319. The full-length PRO1568 protein shown in Figure 154 has an estimated molecular weight of about 35,383 daltons and a pI of about 5.99.

35 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 154 (SEQ ID NO:273), revealed sequence identity between the PRO1568 amino acid sequence and the following Dayhoff sequences (incorporated herein):

AF089749_1, AF054841_1, NAG2_HUMAN, CD63_HUMAN, CD82_HUMAN, P_W05732, P_R86834, A15_HUMAN, P_W27333 and CD37_HUMAN.

EXAMPLE 81: Isolation of cDNA clones Encoding Human PRO1570

5 A consensus DNA sequence encoding PRO1570 was assembled relative to other EST sequences using phrap as described in Example 1 above to form an assembly. This consensus sequence is designated herein as "DNA65415". Based on the DNA65415 consensus sequence and other discoveries and information provided herein, the clone including Incyte EST 3232285 (from a uterine/colon cancer tissue library) was purchased and sequenced in full which gave SEQ ID NO:274.

10 The entire coding sequence of PRO1570 is included in Figure 155 (SEQ ID NO:274). Clone DNA68885-1678 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 210-212 and an apparent stop codon at nucleotide positions 1506-1508 of SEQ ID NO:274. The predicted polypeptide precursor is 432 amino acids long. Figure 275 shows a number of motifs. Clone DNA68885-1678 has been deposited with the ATCC and is assigned ATCC deposit no. 203311. The full-length PRO1570 protein shown in Figure 156 has an estimated molecular weight of about 47,644 daltons and a pI of
15 about 5.18.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 156 (SEQ ID NO:275), revealed sequence identity between the PRO1570 amino acid sequence and the following Dayhoff sequences (incorporated herein): P_W22986, TMS2_HUMAN, HEPS_HUMAN, P_R89435, AB002134_1, KAL_MOUSE, ACRO_HUMAN,
20 GEN12917, AF045649_1, and P_W34285.

EXAMPLE 82: Isolation of cDNA clones Encoding Human PRO1317

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "Consen8865". In addition, the Consen8865
25 consensus sequence was extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is designated herein as "DNA63334". Based on the DNA63334 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1317.

30 PCR primers (forward and reverse) were synthesized:

forward PCR primer: CTGCTGGTGAAATCTGGCGTGGAG (63334.f1; SEQ ID NO:278); and

reverse PCR primer: GTCTGGTCCTGGCTGTCCACCCAG (63334.r1; SEQ ID NO:279).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA63334 sequence which had the following nucleotide sequence:

35 hybridizationprobe: CATCTTGTCATGTACCTGGGAACCACCACAGGGTCGCTCCACAAG(63334.p1; SEQ ID NO:280).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1317 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human hippocampal tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1317 (designated herein as DNA71166-1685 [Figure 157, SEQ ID NO:276]; and the derived protein
5 sequence for PRO1317.

The entire coding sequence of PRO1317 is shown in Figure 157 (SEQ ID NO:276). Clone DNA71166-1685 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 105-107 and an apparent stop codon at nucleotide positions 2388-2390. The predicted polypeptide precursor is 761 amino acids long and has an estimated molecular weight of about 83,574 daltons and a pI of about 6.78.

10 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 158 (SEQ ID NO:277), revealed significant homology between the PRO1317 amino acid sequence and Dayhoff sequence no. I48745. Homology was also revealed between the PRO1317 amino acid sequence the following Dayhoff sequences: I48746, GEN13418, P_W58540, P_217657, MUSC1_1, P_471380, U73167_5, HSU33920_1, and GG828240_1.

15 Clone DNA71166-1685 was deposited with the ATCC on October 20, 1998, and is assigned ATCC deposit no. 203355.

EXAMPLE 83: Isolation of cDNA clones Encoding Human PRO1780

The DNA63837.init sequence was obtained as described in Example 1 above and was extended using
20 repeated cycles of BLAST and the program "phrap" (Phil Green, University of Washington, Seattle) to extend the consensus sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is designated herein as "DNA63837". Based on the DNA63837 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1780.

25 PCR primers (forward and reverse) were synthesized:

forward PCR primer: TGCCTTTGCTCACCTACCCCAAGG (63837.f1; SEQ ID NO:283)

reverse PCR primer: TCAGGCTGGTCTCCAAAGAGAGGG (63837.r1; SEQ ID NO:284)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA63837 sequence which had the following nucleotide sequence:

30 hybridization probe: CCCAAAGATGTCCACCTGGCTGCAAATGTGAAAATTGTGGACTGG (63837.p1; SEQ ID NO:285)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1780 gene using the probe oligonucleotide and one of the PCR primers. RNA
35 for construction of the cDNA libraries was isolated from a human fetal kidney.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1780 (designated herein as DNA71169-1709 [Figure 159, SEQ ID NO:281]; and the derived protein

sequence for PRO1780.

The entire coding sequence of PRO1780 is shown in Figure 159 (SEQ ID NO:281). Clone DNA71169-1709 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 68-70 and an apparent stop codon at nucleotide positions 1637-1639. The predicted polypeptide precursor is 523 amino acids long. The full-length PRO1780 protein shown in Figure 160 has an estimated molecular weight of about 59,581 daltons and a pI of about 8.68. Additional features include a signal peptide sequence at about amino acids 1-19; a transmembrane domain at about amino acids 483-504; tyrosine phosphorylation sites at about amino acids 68-74 and 425-433; N-myristoylation sites at about amino acids 16-21, 301-206, 370-375, and 494-499; and a leucine zipper pattern at about amino acids 493-514.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 160 (SEQ ID NO:282), revealed significant homology between the PRO1780 amino acid sequence and the following Dayhoff sequences: UDA2_RABIT, CGT_HUMAN, UD11_HUMAN, P_R26153, UDB1_RAT, HSU59209_1, AB010872_1, UDB5_MOUSE, UDB8_HUMAN, and UD14_HUMAN.

Clone DNA71169-1709 was deposited with the ATCC on November 17, 1998, and is assigned ATCC deposit no. 203467.

EXAMPLE 84: Isolation of cDNA clones Encoding Human PRO1486

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "DNA48897". Based on the DNA48897 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1486.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'AGGCAGCCACCAGCTCTGTGCTAC3' (SEQ ID NO:288); and
reverse PCR primer 5'CAGAGAGGGAAGATGAGGAAGCCAGAG3' (SEQ ID NO:289).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA48897 sequence which had the following nucleotide sequence:

hybridization probe 5'CTGTGCTACTGCCCTTGGACCCTGGGGACCGAGTGTCTCTGC3' (SEQ ID NO:290).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1486 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from a human adenocarcinoma cell line.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1486 and the derived protein sequence for PRO1486.

The entire coding sequence of PRO1486 is included in Figure 161 (SEQ ID NO:286). Clone DNA71180-1655 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 472-474 and an apparent stop codon at nucleotide positions 1087-1089 of SEQ ID NO:286. The predicted polypeptide precursor is 205 amino acids long. The signal peptide is at about amino acids 1-32 of SEQ ID NO:287. Regions similar to those of C1q and an N-glycosylation site are located as indicated in Figure 162. Clone DNA71180-1655 has been deposited with the ATCC and is assigned ATCC deposit no. 203403. The full-length PRO1486 protein shown in Figure 162 has an estimated molecular weight of about 21,521 daltons and a pI of about 7.07.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 162 (SEQ ID NO:287), revealed sequence identity between the PRO1486 amino acid sequence and the following Dayhoff sequences: CERB_HUMAN, CERL_RAT, GEN11893, P_R22263, CA18_HUMAN, C1QC_HUMAN, AF054891_1, A57131, HUMC1Qb2_1, ACR3_MOUSE.

EXAMPLE 85: Isolation of cDNA clones Encoding Human PRO1433

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA45230. Based on the DNA45230 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1433.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (45230.fl) 5'-GCTGACCTGGTTCCCATCTACTCC-3' (SEQ ID NO:293)
reverse PCR primer (45230.rl) 5'-CCCACAGACACCCATGACACTTCC-3' (SEQ ID NO:294)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45230 sequence which had the following nucleotide sequence

hybridization probe (45230.pl)

5'-AAGAATGAATTGTACAAAGCAGGTGATCTTCGAGGAGGGCTCCTGGGGCC-3' (SEQ ID NO:295)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1433 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human adrenal gland tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1433 (designated herein as DNA71184-1634 [Figure 163, SEQ ID NO:291]; and the derived protein sequence for PRO1433.

The entire nucleotide sequence of DNA71184-1634 is shown in Figure 163 (SEQ ID NO:291). Clone DNA71184-1634 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 185-187 and ending at the stop codon at nucleotide positions 1349-1351 (Figure 163). The predicted polypeptide precursor is 388 amino acids long (Figure 164). The full-length PRO1433 protein shown in Figure 164 has an estimated molecular weight of about 43,831 daltons and a pI of about 9.64. Analysis of the full-length PRO1433 sequence shown in Figure 164 (SEQ ID NO:292) evidences the presence of the following: a

transmembrane domain from about amino acid 76 to about amino acid 97, potential N-glycosylation sites from about amino acid 60 to about amino acid 63, from about amino acid 173 to about amino acid 176 and from about amino acid 228 to about amino acid 231 and potential N-myristolation sites from about amino acid 10 to about amino acid 15, from about amino acid 41 to about amino acid 46, from about amino acid 84 to about amino acid 89, from about amino acid 120 to about amino acid 125, from about amino acid 169 to about amino acid 174, from about amino acid 229 to about amino acid 234, from about amino acid 240 to about amino acid 245, from about amino acid 318 to about amino acid 323 and from about amino acid 378 to about amino acid 383. Clone DNA71184-1634 has been deposited with ATCC on September 22, 1998 and is assigned ATCC deposit no. 203266.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 164 (SEQ ID NO:292), evidenced significant homology between the PRO1433 amino acid sequence and the following Dayhoff sequences: CELW01A11_4, CEF59A1_4, S67138, MTV050_3, S75135 and S12411.

EXAMPLE 86: Isolation of cDNA clones Encoding Human PRO1490

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA67006. Based on the DNA67006 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1490.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (67006.f1) 5'-CTTCCTCTGTGGGTGGACCATGTG-3' (SEQ ID NO:298)

reverse PCR primer (67006.r1) 5'-GCCACCTCCATGCTAACGCGG-3' (SEQ ID NO:299)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA67006 sequence which had the following nucleotide sequence

hybridization probe (67006.p1)

5'-CCAAGGTCCTCGCTAAGAAGGAGCTGCTCTACGTGCCCCTCATCG-3' (SEQ ID NO:300)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1490 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human adrenal gland tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1490 (designated herein as DNA71213-1659 [Figure 165, SEQ ID NO:296]; and the derived protein sequence for PRO1490.

The entire nucleotide sequence of DNA71213-1659 is shown in Figure 165 (SEQ ID NO:296). Clone DNA71213-1659 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 272-274 and ending at the stop codon at nucleotide positions 1376-1378 (Figure 165). The predicted polypeptide precursor is 368 amino acids long (Figure 166). The full-length PRO1490 protein shown in Figure

166 has an estimated molecular weight of about 42,550 daltons and a pI of about 9.11. Analysis of the full-length PRO1490 sequence shown in Figure 166 (SEQ ID NO:297) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25, transmembrane domains from about amino acid 307 to about amino acid 323 and from about amino acid 335 to about amino acid 352 and tyrosine kinase phosphorylation sites from about amino acid 160 to about amino acid 168 and from about amino acid 161 to about amino acid 168. Clone DNA71213-1659 has been deposited with ATCC on October 27, 1998 and is assigned ATCC deposit no. 203401.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 166 (SEQ ID NO:297), evidenced significant homology between the PRO1490 amino acid sequence and the following Dayhoff sequences: A52744_1, S60478, P_R99249, P_R59712, YBP2_YEAST, S54641, CELT05H4_15, CELF28B3_1, CELZK40_1 and YIHG_ECOLI.

EXAMPLE 87: Isolation of cDNA clones Encoding Human PRO1482

A cDNA clone (DNA71234-1651) encoding a native human PRO1482 polypeptide was identified by a yeast screen, in a human adrenal gland cDNA library that preferentially represents the 5' ends of the primary cDNA clones.

The full-length DNA71234-1651 clone shown in Figure 167 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 33-35 and ending at the stop codon at nucleotide positions 462-464 (Figure 167). The predicted polypeptide precursor is 143 amino acids long (Figure 168). The full-length PRO1482 protein shown in Figure 168 has an estimated molecular weight of about 15,624 daltons and a pI of about 9.58. Analysis of the full-length PRO1482 sequence shown in Figure 168 (SEQ ID NO:302) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28. Clone DNA71234-1651 has been deposited with ATCC on October 27, 1998 and is assigned ATCC deposit no. 203402.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 168 (SEQ ID NO:302), evidenced significant homology between the PRO1482 amino acid sequence and the following Dayhoff sequences: A18267_3.

EXAMPLE 88: Isolation of cDNA clones Encoding Human PRO1446

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from a pancreatic islet cell library. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green,

University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56514.

In light of the sequence homology between the DNA56514 sequence and an EST sequence contained within the Incyte EST 2380344, the clone including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 169 and is herein designated as
5 DNA71277-1636.

The full length clone shown in Figure 169 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 152-154 and ending at the stop codon found at nucleotide positions 479-481 (Figure 169; SEQ ID NO:303). The predicted polypeptide precursor (Figure 170, SEQ ID NO:304) is 109 amino acids long with a signal peptide at about amino acids 1-15 of SEQ ID NO:304. PRO1446
10 has a calculated molecular weight of approximately 11,822 daltons and an estimated pI of approximately 8.63. Clone DNA71277-1636 was deposited with the ATCC on September 22, 1998 and is assigned ATCC deposit no. 203285.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 170 (SEQ ID NO:304), revealed sequence identity
15 between the PRO1446 amino acid sequence and the following Dayhoff sequences (data incorporated herein): P53_CANFA, P53_FELCA, LRP1_HSV1F, OSU57338_1, S75842, P_P93722, AF002189_1, B70408, S54309 and S53365. The first in this list is further described in Kraegel, et al., Cancer Lett., 92(2):181-186 (1995).

EXAMPLE 89: Isolation of cDNA clones Encoding Human PRO1558

20 Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 86390. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST
25 or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA58842.

In light of the sequence homology between the DNA58842 sequence and an EST sequence contained
30 within the Incyte EST clone no. 3746964, the Incyte EST clone no. 3746964 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 171 and is herein designated as DNA71282-1668.

Clone DNA71282-1668 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 84-86 and ending at the stop codon at nucleotide positions 870-872 (Figure 171). The
35 predicted polypeptide precursor is 262 amino acids long (Figure 172). The full-length PRO1558 protein shown in Figure 172 has an estimated molecular weight of about 28,809 daltons and a pI of about 8.80. Analysis of the full-length PRO1558 sequence shown in Figure 172 (SEQ ID NO:306) evidences the presence of the

following: a signal peptide from about amino acid 1 to about amino acid 25, transmembrane domains from about amino acid 8 to about amino acid 30 and from about amino acid 109 to about amino acid 130, a potential N-glycosylation site from about amino acid 190 to about amino acid 193, a tyrosine kinase phosphorylation site from about amino acid 238 to about amino acid 246, potential N-myristylation sites from about amino acid 22 to about amino acid 27, from about amino acid 28 to about amino acid 33, from about amino acid 110 to about amino acid 115, from about amino acid 205 to about amino acid 210 and from about amino acid 255 to about amino acid 260 and amidation sites from about amino acid 31 to about amino acid 34 and from about amino acid 39 to about amino acid 42. Clone DNA71282-1668 has been deposited with ATCC on October 6, 1998 and is assigned ATCC deposit no. 203312.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 172 (SEQ ID NO:306), evidenced significant homology between the PRO1558 amino acid sequence and the following Dayhoff sequences: AF075724_2, MXU24657_3, CAMT_EUCGU, MSU20736_1, P_R29515, B70431, JC4004, CEY32B12A_3, CELF53B3_2 and P_R13543.

15 EXAMPLE 90: Isolation of cDNA clones Encoding Human PRO1604

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched. Incyte EST No. 3550440 was identified as having homology to HDGF. EST No. 3550440 was then compared to various EST databases including public EST databases (e.g. GenBank), and the LIFESEQ® database, to identify homologous EST sequences. The search was performed using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is designated herein "DNA67237".

In light of the sequence homology between the DNA67237 sequence and EST no. 3367060 from the LIFESEQ® database, the clone containing Incyte EST No. 3367060 was purchased and the cDNA insert was obtained and sequenced to obtain the entire coding sequence of PRO1604 which is shown in Figure 173 (SEQ ID NO:307).

Clone DNA71286-1687 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 65-67 and an apparent stop codon at nucleotide positions 2078-2080. The predicted polypeptide precursor is 671 amino acids long. The full-length PRO1604 protein shown in Figure 174 has an estimated molecular weight of about 74,317 daltons and a pI of about 7.62. Additional features include a signal peptide at about amino acids 1-13; potential cAMP- and cGMP-dependent protein kinase phosphorylation sites at about amino acids 156-159, 171-174, and 451-454; potential N-myristoylation sites at about amino acids 46-51, 365-370, and 367-372; and a cell attachment sequence at about amino acids 661-663.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 174 (SEQ ID NO:308), revealed significant homology between the PRO1604 amino acid sequence and Dayhoff sequence no. P_W37483. Homology was

also shown between the PRO1604 amino acid sequence and the following additional Dayhoff sequences: AF063020_1, P_R66727, P_W37482, JC5661, CEC25A1_11, CEU33058_1, I38073, MST2_DROHY, and HSATRX36_1.

Clone DNA71286-1687 was deposited with the ATCC on October 20, 1998, and is assigned ATCC deposit no. 203357.

5

EXAMPLE 91: Isolation of cDNA clones Encoding Human PRO1491

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA67202. Based on the DNA67202 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained
10 the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1491.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (67202.f1) 5'-CAACGCAGCCGTGATAACAAGTGG-3' (SEQ ID NO:311)

reverse PCR primer (67202.r1) 5'-GCTTGGACATGTACCAGGCCGTGG-3' (SEQ ID NO:312)

15 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA67202 sequence which had the following nucleotide sequence

hybridization probe (67202.p1)

5'-GGCCAGACTGATTTGCTCAATTCCTGGAAGTGATGGGGCAGATAC-3' (SEQ ID NO:313)

RNA for construction of the cDNA libraries was isolated from human aortic endothelial cell tissue.

20 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1491 (designated herein as DNA71883-1660 [Figure 175, SEQ ID NO:309]; and the derived protein sequence for PRO1491.

The entire nucleotide sequence of DNA71883-1660 is shown in Figure 175 (SEQ ID NO:309). Clone DNA71883-1660 contains a single open reading frame with an apparent translational initiation site at nucleotide
25 positions 107-109 and ending at the stop codon at nucleotide positions 2438-2440 (Figure 175). The predicted polypeptide precursor is 777 amino acids long (Figure 176). The full-length PRO1491 protein shown in Figure 176 has an estimated molecular weight of about 89,651 daltons and a pI of about 7.97. Analysis of the full-length PRO1491 sequence shown in Figure 176 (SEQ ID NO:310) evidences the presence of the following: a
30 signal peptide from about amino acid 1 to about amino acid 36, potential N-glycosylation sites from about amino acid 139 to about amino acid 142, from about amino acid 607 to about amino acid 610 and from about amino acid 724 to about amino acid 727, a tyrosine kinase phosphorylation site from about amino acid 571 to about amino acid 576 and a gram-positive cocci surface protein anchoring hexapeptide sequence from about amino acid 32 to about amino acid 37. Clone DNA71883-1660 has been deposited with ATCC on November 17, 1998 and is assigned ATCC deposit no. 203475.

35 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 176 (SEQ ID NO:310), evidenced significant homology between the PRO1491 amino acid sequence and the following Dayhoff sequences: GGU28240_1,

MUSC1_1, D49423, MMSEMH_1, AB002329_1, AF022947_1, HSU33920_1, HUMLUCA19_1, G01856 and AF022946_1.

EXAMPLE 92: Isolation of cDNA clones Encoding Human PRO1431

5 An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST (isolated from adult brain stem tissue) was identified (1370141, DNA66505) which showed homology to SH3. RNA for construction of cDNA libraries was isolated from human bone marrow. A full length cDNA corresponding to the isolated EST was isolated using an *in vitro* cloning technique (DNA73401-1633) in pRK5.

10 The cDNA libraries used to isolate the cDNA clones encoding human PRO1431 were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI.

15 A cDNA clone was sequenced in entirety. The entire nucleotide sequence of DNA73401-1633 (SEQ ID NO:314) is shown in Figure 177. Clone DNA73401-1633 contains a single open reading frame with an apparent translational initiation site at about nucleotide positions 630-632 and a stop codon at about nucleotide positions 1740-1742. The predicted polypeptide precursor encoded by DNA73401-1633 is 370 amino acids long. Clone DNA73401 (designated as DNA73402-1633) has been deposited with ATCC and is assigned ATCC
20 deposit no. 203273.

Based sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1431 shows significant amino acid sequence identity to SH17_HUMAN, an SH3 containing protein known as SH3P17. Additional significant identity score were found with D89164_1, AF032118_1, EXLP_TOBAC, YHR4_YEAST, S46992, RATP130CAS_2, AF043259_1, RATP130CAS_1 and MYSC_ACACA.

25

EXAMPLE 93: Isolation of cDNA clones Encoding Human PRO1563

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA67191. Based on the DNA67191 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained
30 the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1563.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (67191.f1) 5'-CCCTGAAGCTGCCAGATGGCTCC-3' (SEQ ID NO:318)

reverse PCR primer (67191.r1) 5'-CTGTGCTCTTCGGTGCAGCCAGTC-3' (SEQ ID NO:319)

35 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA67191 sequence which had the following nucleotide sequence

hybridization probe (67191.p1)

5'-CCACAGATGTGGTACTGCCTGGGGCAGTCAGCTTGCGCTACAG-3' (SEQ ID NO:320)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1563 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow tissue.

5 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1563 (designated herein as DNA73492-1671 [Figures 179A-B, SEQ ID NO:316]; and the derived protein sequence for PRO1563.

The entire nucleotide sequence of DNA73492-1671 is shown in Figures 179A-B (SEQ ID NO:316). Clone DNA73492-1671 contains a single open reading frame with an apparent translational initiation site at
 10 nucleotide positions 419-421 and ending at the stop codon at nucleotide positions 2930-2932 (Figures 179A-B). The predicted polypeptide precursor is 837 amino acids long (Figure 180). The full-length PRO1563 protein shown in Figure 180 has an estimated molecular weight of about 90,167 daltons and a pI of about 8.39. Analysis of the full-length PRO1563 sequence shown in Figure 180 (SEQ ID NO:317) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 48, a potential N-glycosylation site from
 15 about amino acid 68 to about amino acid 71, glycosaminoglycan attachment sites from about amino acid 188 to about amino acid 191 and from about amino acid 772 to about amino acid 775, a cAMP- and cGMP-dependent protein kinase phosphorylation site from about amino acid 182 to about amino acid 185, a tyrosine kinase phosphorylation site from about amino acid 730 to about amino acid 736, potential N-myristylation sites from
 20 about amino acid 5 to about amino acid 10, from about amino acid 19 to about amino acid 24, from about amino acid 121 to about amino acid 126, from about amino acid 125 to about amino acid 130, from about amino acid 130 to about amino acid 135, from about amino acid 147 to about amino acid 152, from about amino acid 167 to about amino acid 172, from about amino acid 168 to about amino acid 173, from about amino acid 174 to about amino acid 179, from about amino acid 323 to about amino acid 328, from about amino acid 352 to about amino acid 357, from about amino acid 539 to about amino acid 544, from about amino acid 555 to about amino
 25 acid 560, from about amino acid 577 to about amino acid 582, from about amino acid 679 to about amino acid 684, from about amino acid 682 to about amino acid 687, and from about amino acid 763 to about amino acid 768, amidation sites from about amino acid 560 to about amino acid 563 and from about amino acid 834 to about amino acid 837, leucine zipper pattern sequences from about amino acid 17 to about amino acid 38 and from about amino acid 24 to about amino acid 45 and a neutral zinc metallopeptidase, zinc-binding region signature
 30 sequence from about amino acid 358 to about amino acid 367. Clone DNA73492-1671 has been deposited with ATCC on October 6, 1998 and is assigned ATCC deposit no. 203324.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 180 (SEQ ID NO:317), evidenced significant homology between the PRO1563 amino acid sequence and the following Dayhoff sequences: AB014588_1,
 35 D67076_1, AB001735_1, P_W47028, AB002364_1, P_W47029, GEN13695, P_R40823, AF005665_1 and DISA_TRIGA.

EXAMPLE 94: Isolation of cDNA clones Encoding Human PRO1565

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA67183. Based on an observed homology between the DNA67183 consensus sequence and an EST sequence contained within Incyte EST clone no. 2510320, Incyte EST clone no. 2510320 was purchased and its insert was obtained and sequenced. That
 5 insert sequence is shown in Figure 181 and is herein designated DNA73727-1673 (SEQ ID NO:321).

The entire nucleotide sequence of DNA73727-1673 is shown in Figure 181 (SEQ ID NO:321). Clone DNA73727-1673 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 59-61 and ending at the stop codon at nucleotide positions 1010-1012 (Figure 181). The predicted polypeptide precursor is 317 amino acids long (Figure 182). The full-length PRO1565 protein shown in Figure
 10 182 has an estimated molecular weight of about 37,130 daltons and a pI of about 5.18. Analysis of the full-length PRO1565 sequence shown in Figure 182 (SEQ ID NO:322) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 40, a potential type II transmembrane domain from about amino acid 25 to about amino acid 47, potential N-glycosylation sites from about amino acid 94 to about amino acid 97 and from about amino acid 180 to about amino acid 183, glycosaminoglycan attachment sites from
 15 about amino acid 92 to about amino acid 95, from about amino acid 70 to about amino acid 73, from about amino acid 85 to about amino acid 88, from about amino acid 133 to about amino acid 136, from about amino acid 148 to about amino acid 151, from about amino acid 192 to about amino acid 195 and from about amino acid 239 to about amino acid 242, potential N-myristolation sites from about amino acid 33 to about amino acid 38, from about amino acid 95 to about amino acid 100, from about amino acid 116 to about amino acid 121,
 20 from about amino acid 215 to about amino acid 220 and from about amino acid 272 to about amino acid 277, a microbodies C-terminal targeting signal sequence from about amino acid 315 to about amino acid 317 and a cytochrome C family heme-binding site signature sequence from about amino acid 9 to about amino acid 14. Clone DNA73727-1673 has been deposited with ATCC on November 3, 1998 and is assigned ATCC deposit no. 203459.

25 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 182 (SEQ ID NO:322), evidenced significant homology between the PRO1565 amino acid sequence and the following Dayhoff sequences: AF051425_1, P_R65490, P_R65488, GRPE_STAAU, RNU31330_1, ACCD_BRANA, D50558_1, HUMAMYAB3_1, P_W34452 and P_P50629.

30

EXAMPLE 95: Isolation of cDNA clones Encoding Human PRO1571

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA69559. Based on homology observed between the DNA69559 consensus sequence and an EST sequence contained within the Incyte EST clone no.
 35 3140760, Incyte EST clone no. 3140760 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 183 and is herein designated as DNA73730-1679.

Clone DNA73730-1679 contains a single open reading frame with an apparent translational initiation

site at nucleotide positions 90-92 and ending at the stop codon at nucleotide positions 807-809 (Figure 183). The predicted polypeptide precursor is 239 amino acids long (Figure 184). The full-length PRO1571 protein shown in Figure 184 has an estimated molecular weight of about 25,699 daltons and a pI of about 8.99. Analysis of the full-length PRO1571 sequence shown in Figure 184 (SEQ ID NO:324) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21 and transmembrane domains from about amino acid 82 to about amino acid 103, from about amino acid 115 to about amino acid 141 and from about amino acid 160 to about amino acid 182. Clone DNA73730-1679 has been deposited with ATCC on October 6, 1998 and is assigned ATCC deposit no. 203320.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 184 (SEQ ID NO:324), evidenced significant homology between the PRO1571 amino acid sequence and the following Dayhoff sequences: AF072128_1, AB000712_1, AB000714_1, AF007189_1, AF000959_1, AF068863_1, P_W15288, PM22_HUMAN, P_R30056 and LSU46824_1.

EXAMPLE 96: Isolation of cDNA clones Encoding Human PRO1572

Using the method described in Example 1 above, a consensus sequence was obtained. The consensus sequence is designated herein "DNA69560". Based on the DNA69560 consensus sequence and other information provided herein, a clone including another EST (Incyte DNA3051424) from the assembly was purchased and sequenced.

The entire coding sequence of PRO1573 is included in Figure 185 (SEQ ID NO:325). Clone DNA73734-1680 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 90-92 and an apparent stop codon at nucleotide positions 873-875. The predicted polypeptide precursor is 261 amino acids long. The signal peptide is at about amino acids 1-23 and the transmembrane domains are at about amino acids 81-100, 121-141, and 173-194 of SEQ ID NO:326. One or more of the transmembrane domains can be deleted or inactivated. The locations of a N-glycosylation site, N-myristoylation sites, a tyrosine kinase phosphorylation site and a prokaryotic membrane lipoprotein lipid attachment site are indicated in Figure 186. Clone DNA73734-1680 has been deposited with the ATCC and is assigned ATCC deposit no. 203363. The full-length PRO1572 protein shown in Figure 186 has an estimated molecular weight of about 27,856 daltons and a pI of about 8.5.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 186 (SEQ ID NO:326), revealed sequence identity between the PRO1572 amino acid sequence and the following Dayhoff sequences (incorporated herein): AF072127_1, HSU89916_1, AB000713_1, AB000714_1, AB000712_1, AF000959_1, AF072128_1, AF068863_1, P_W29881, and P_W58869.

EXAMPLE 97: Isolation of cDNA clones Encoding Human PRO1573

EST 3628990 was identified in an Incyte Database, (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) and extended in a comparison to other sequences in databases to form an assembly. The alignment search

was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence is designated herein
5 "DNA69561".

Based on the DNA69561 consensus sequence and other information provided herein, a clone including another EST (Incyte DNA3752657) from the assembly was purchased and sequenced. This clone came from a breast tumor tissue library.

The entire coding sequence of PRO1573 is included in Figure 187 (SEQ ID NO:327). Clone
10 DNA73735-1681 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 97-99 and an apparent stop codon at nucleotide positions 772-774. The predicted polypeptide precursor is 225 amino acids long. The signal peptide is at about amino acids 1-17 and the transmembrane domains are at about amino acids 82-101, 118-145, and 164-188 of SEQ ID NO:328. One or more of the transmembrane domains can be deleted or inactivated. A phosphorylation site, amidation site, and N-myristoylation sites are
15 shown in Figure 188. Clone DNA73735-1681 has been deposited with ATCC and is assigned ATCC deposit no. 203356. The full-length PRO1573 protein shown in Figure 188 has an estimated molecular weight of about 24,845 daltons and a pI of about 9.07.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 188 (SEQ ID NO:328), revealed sequence identity
20 between the PRO1573 amino acid sequence and the following Dayhoff sequences (incorporated herein): AF007189_1, AB000714_1, AB000713_1, AB000712_1, A39484, AF000959_1, AF072127_, AF072128_1, AF068863_1 and AF077739_1.

EXAMPLE 98: Isolation of cDNA clones Encoding Human PRO1488

25 An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and EST No. 3639112H1 was identified as having homology to CPE-R. EST No. 3639112H1 is designated herein as "DNA69562". EST clone 3639112H1, which was derived from a lung tissue library of a 20-week old fetus who died from Patau's syndrome, was purchased and the cDNA insert was obtained and sequenced in its entirety. The entire nucleotide sequence of PRO1488 is shown in Figure 189 (SEQ ID
30 NO:329), and is designated herein as DNA73736-1657. DNA73736-1657 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 6-8 and a stop codon at nucleotide positions 666-668 (Figure 189; SEQ ID NO:329). The predicted polypeptide precursor is 220 amino acids long.

The full-length PRO1488 protein shown in Figure 190 has an estimated molecular weight of about 23,292 daltons and a pI of about 8.43. Four transmembrane domains have been identified as being located at
35 about amino acid positions 8-30, 82-102, 121-140, and 166-186.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 190 (SEQ ID NO:330), revealed significant

homology between the PRO1488 amino acid sequence and Dayhoff sequence AB000712_1. Homology was also found between the PRO1488 amino acid sequence and the following additional Dayhoff sequences: AB000714_1, AF007189_1, AF000959_1, P_W63697, MMU82758_1, AF072127_1, AF072128_1, HSU89916_1, AF068863_1, CEAFO00418_1, and AF077739_1.

5 Clone DNA73736-1657 was deposited with the ATCC on November 17, 1998, and is assigned ATCC deposit no. 203466.

EXAMPLE 99: Isolation of cDNA clones Encoding Human PRO1489

10 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA69563. Based upon an observed sequence similarity between the DNA69563 consensus sequence and an EST sequence contained within the Incyte EST clone no. 3376608, Incyte EST clone no. 3376608 was purchased and its insert obtained and sequenced. That insert is herein designated DNA73737-1658.

15 The entire nucleotide sequence of DNA73737-1658 is shown in Figure 191 (SEQ ID NO:331). Clone DNA73737-1658 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 264-266 and ending at the stop codon at nucleotide positions 783-785 (Figure 191). The predicted polypeptide precursor is 173 amino acids long (Figure 192). The full-length PRO1489 protein shown in Figure 192 has an estimated molecular weight of about 18,938 daltons and a pI of about 9.99. Analysis of the full-length PRO1489 sequence shown in Figure 192 (SEQ ID NO:332) evidences the presence of the following: transmembrane domains from about amino acid 31 to about amino acid 51, from about amino acid 71 to about amino acid 90 and from about amino acid 112 to about amino acid 133 and a potential N-glycosylation site from about amino acid 161 to about amino acid 164. Clone DNA73737-1658 has been deposited with ATCC on 20 October 27, 1998 and is assigned ATCC deposit no. 203412.

25 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 192 (SEQ ID NO:332), evidenced significant homology between the PRO1489 amino acid sequence and the following Dayhoff sequences: AF007189_1, AB000712_1, AF000959_1, MMU82758_1, AF035814_1, AF072127_1, AF072128_1, HSU89916_1, AF068863_1 and PPU50051_1.

EXAMPLE 100: Isolation of cDNA clones Encoding Human PRO1474

30 An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified. This EST showed homology to pancreatic secretory trypsin inhibitor.

The clone which included this EST was purchased from Incyte (it came from a uterine cervical tissue library) and sequenced in full to reveal the nucleic acid of SEQ ID NO:333, which encodes PRO1474.

35 The entire nucleotide sequence of PRO1474 is shown in Figure 193 (SEQ ID NO:333). Clone DNA73739-1645 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 45-47 and a stop codon at nucleotide positions 300-302 (Figure 193; SEQ ID NO:333). The predicted polypeptide precursor is 85 amino acids long. As indicated in Figure 194, the Kazal serine protease inhibitor

family signature begins at about amino acid 45 of SEQ ID NO:334. Also indicated in Figure 194 is a region conserved in integrin alpha chains (beginning at about amino acid 32 of SEQ ID NO:334). Clone DNA73739-1645 has been deposited with the ATCC and is assigned ATCC deposit no. 203270. The full-length PRO1474 protein shown in Figure 194 has an estimated molecular weight of about 9,232 daltons and a pI of about 7.94.

5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 194 (SEQ ID NO:334), revealed sequence identity between the PRO1474 amino acid sequence and the following Dayhoff sequences (all ovomucoids, data incorporated herein by reference): IOVO_FRAER, IOVO_FRAAF, IOVO_FRACO, IOVO_CYRMO, IOVO_STRCA, H61492, C61589, IOVO_POLPL, D61589, and IOVO_TURME.

10 EXAMPLE 101: Isolation of cDNA clones Encoding Human PRO1508

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte Cluster No. 34523, also referred herein as "DNA10047". This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public and private EST databases (e.g., GenBank and (LIFESEQ®) to identify existing
15 homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated "DNA55723".

20 In light of the sequence homology between the DNA55723 sequence a sequence contained within Incyte EST no. 2989064, the EST clone 2989064 was purchased and the cDNA insert was obtained and sequenced in its entirety. The sequence of this cDNA insert is shown in Figure 195 and is herein designated as "DNA73742-1662".

The full length clone shown in Figure 195 contained a single open reading frame with an apparent
25 translational initiation site at nucleotide positions 70 to 72 and ending at the stop codon found at nucleotide positions 514 to 516 (Figure 195; SEQ ID NO:335). The predicted polypeptide precursor (Figure 196, SEQ ID NO:335) is 148 amino acids long. Other features of the PRO1508 protein include: a signal sequence at about amino acids 1-30; a tyrosine kinase phosphorylation motif at about amino acids 96-103; and N-myristoylation motifs at about amino acids 27-32, 28-33, and 140-145. PRO1508 has a calculated molecular weight of
30 approximately 17,183 daltons and an estimated pI of approximately 8.77. Clone DNA73742-1662 was deposited with the ATCC on October 6, 1998 and is assigned ATCC deposit no. 203316.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 196 (SEQ ID NO:336), revealed some homology between the PRO1508 amino acid sequence and the following Dayhoff sequences: HSAJ3728_1; P_R74962;
35 P_R74941; AF053074_1; F69515; S20706; RPB1_PLAFD; A20587_1; A51861_1; and S75947.

EXAMPLE 102: Isolation of cDNA clones Encoding Human PRO1555

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated EST cluster no. 521, and also referred to herein as "DNA10316". This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and the LIFESEQ® database to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated "DNA56374".

10 In light of the sequence homology between the DNA56374 sequence and an EST sequence contained within Incyte EST no.2855769, EST no.2855769 was purchased and the cDNA insert was obtained and sequenced. EST no. 2855769 was derived from a library constructed from female breast fat tissue. The sequence of this cDNA insert is shown in Figure 197 and is herein designated as DNA73744-1665.

The full length clone shown in Figure 197 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 90 to 92 and ending at the stop codon found at nucleotide positions 828 to 830 (Figure 197; SEQ ID NO:337). The predicted polypeptide precursor (Figure 198, SEQ ID NO:338) is 246 amino acids long. PRO1555 has a calculated molecular weight of approximately 26,261 daltons and an estimated pI of approximately 5.65. Additional features include: a signal peptide at about amino acids 1-31; transmembrane domains at about amino acids 11-31 and 195-217; a potential N-glycosylation site at about amino acids 111-114; potential casein kinase II phosphorylation sites at about amino acids 2-5, 98-101, and 191-194; and potential N-myristoylation sites at about amino acids 146-151, and 192-197.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 198 (SEQ ID NO:338), revealed some homology between the PRO1555 amino acid sequence and the following Dayhoff sequences: YKA4_CAEEL, AB014541_1, HVSX99518_2, SSU63019_1, GEN14286, MMU68267_1, XP2_XENLA, ICP4_HSV11, P_W40200, and AE001360_1.

Clone DNA73744-1665 was deposited with the ATCC on October 6, 1998, and is assigned ATCC deposit no. 203322.

30 EXAMPLE 103: Isolation of cDNA clones Encoding Human PRO1485

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "DNA44791". Based on the DNA44791 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1485.

PCR primers (2 forward and 2 reverse) were synthesized:
forward PCR primer 1: 5'CCCTCCAAGGATGACAAAGGCGC 3' (SEQ ID NO:341);

forward PCR primer 2: 5'GGTCAGCAGCTTTCTTGCCCTAAATCAGG 3' (SEQ ID NO:342);
reverse PCR primer 1: 5'ATCTCAGGCGGCATCCTGTCAGCC 3' (SEQ ID NO:343); and
reverse PCR primer 2: 5'GTGGATGCCTGCAAGAAGGTTGGG 3' (SEQ ID NO:344).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA44791 sequence which had the following nucleotide sequence:

5 hybridization probe 5'AGCTTTCTTGCCCTAAATCAGGCCAGCCTCATCAGTCGCTGTGAC 3' (SEQ ID NO:345)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1485 gene using the probe oligonucleotide and one of the PCR primers. RNA
 10 for construction of the cDNA libraries was isolated from human testis.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1485 (designated herein as DNA73746-1654 [Figure 199, SEQ ID NO:339]; and the derived protein sequence for PRO1485.

The entire coding sequence of PRO1485 is shown in Figure 199 (SEQ ID NO:339). Clone DNA73746-
 15 1654 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 151-153 and an apparent stop codon at nucleotide positions 595-597 of SEQ ID NO:339. The predicted polypeptide precursor is 148 amino acids long. The signal peptide is at about amino acids 1-18 of SEQ ID NO:340. The lysozyme C signature, CAAX box, and an N-glycosylation site are shown in Figure 200. Clone DNA73746-1654 has been deposited with ATCC and is assigned ATCC deposit no. 203411. The full-length
 20 PRO1485 protein shown in Figure 200 has an estimated molecular weight of about 16,896 daltons and a pI of about 6.05.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 200 (SEQ ID NO:340), revealed sequence identity between the PRO1485 amino acid sequence and the following Dayhoff sequences: LYC_PHACO, P_R76684,
 25 2HFL_Y, JC2144, JC5544, JC5555, JC5369, LYC2_PIG, P_R12113, and JC5380.

EXAMPLE 104: Isolation of cDNA clones Encoding Human PRO1564

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA67213. Based on the DNA67213
 30 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1564.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (67213.f1) 5'-GGAGAGGTGGTGGCCATGGACAG-3' (SEQ ID NO:348)
 35 reverse PCR primer (67213.r1) 5'-CTGTCAGTCAAGGAGCCAACACC-3' (SEQ ID NO:349)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA67213 sequence which had the following nucleotide sequence

hybridization probe (67213.pl)

5'-TATGTCGCTGCGAGGTGGTGAAAACCTCGAACTGTCTTTCAAGGC-3' (SEQ ID NO:350)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1564 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast carcinoma tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1564 (designated herein as DNA73760-1672 [Figure 201, SEQ ID NO:346]; and the derived protein sequence for PRO1564.

The entire nucleotide sequence of DNA73760-1672 is shown in Figure 201 (SEQ ID NO:346). Clone DNA73760-1672 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 462-464 and ending at the stop codon at nucleotide positions 2379-2381 (Figure 201). The predicted polypeptide precursor is 639 amino acids long (Figure 202). The full-length PRO1564 protein shown in Figure 202 has an estimated molecular weight of about 73,063 daltons and a pI of about 6.84. Analysis of the full-length PRO1564 sequence shown in Figure 202 (SEQ ID NO:347) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, a transmembrane domain from about amino acid 11 to about amino acid 36, potential N-glycosylation sites from about amino acid 107 to about amino acid 110 and from about amino acid 574 to about amino acid 577, a tyrosine kinase phosphorylation site from about amino acid 50 to about amino acid 57, potential N-myristoylation sites from about amino acid 158 to about amino acid 163, from about amino acid 236 to about amino acid 241, from about amino acid 262 to about amino acid 267, from about amino acid 270 to about amino acid 275, from about amino acid 380 to about amino acid 385 and from about amino acid 513 to about amino acid 518, an amidation site from about amino acid 110 to about amino acid 113 and a prokaryotic membrane lipoprotein lipid attachment site from about amino acid 15 to about amino acid 25. Clone DNA73760-1672 has been deposited with ATCC on October 6, 1998 and is assigned ATCC deposit no.203314.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 202 (SEQ ID NO:347), evidenced significant homology between the PRO1564 amino acid sequence and the following Dayhoff sequences: MMU73819_1, HSY08564_1, P_W34470, P_R66402, PAGT_HUMAN, CEGLY5B_1, CEGLY6A_1, CEGLY6B_1, AP000006_308 and E69322.

EXAMPLE 105: Isolation of cDNA clones Encoding Human PRO1755

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated EST Cluster No. 141872. This EST cluster sequence was then compared to a variety of ESTs from the databases listed above to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with

the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated "DNA55731".

In light of the sequence homology between the DNA55731 sequence and a sequence contained within Incyte EST no. 257323, the EST clone was purchased and the cDNA insert was obtained and sequenced. Incyte clone 257323 was derived from a library constructed using RNA isolated from the hNT2 cell line (Stratagene library no. STR9372310), which was derived from a human teratocarcinoma that exhibited properties characteristic of a committed neuronal precursor at an early stage of development. The sequence of this cDNA insert is shown in Figure 203 and is herein designated "DNA76396-1698". Alternatively, the DNA76396-1698 sequence can be obtained by preparing oligonucleotide probes and primers and isolating the sequence from an appropriate library (e.g. STR9372310).

The full length clone shown in Figure 203 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 58 to 60 and ending at the stop codon found at nucleotide positions 886 to 888 (Figure 203; SEQ ID NO:351). The predicted polypeptide precursor (Figure 204, SEQ ID NO:352) is 276 amino acids long. PRO1755 has a calculated molecular weight of approximately 29,426 daltons and an estimated pI of approximately 9.40. Additional features include: a signal peptide sequence at about amino acids 1-31; a transmembrane domain at about amino acids 178-198; a cAMP and cGMP-dependent protein kinase phosphorylation site at about amino acids 210-213; potential N-myristoylation sites at about amino acids 117-122, 154-149, and 214-219; and a cell attachment sequence at about amino acids 149-151.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 204 (SEQ ID NO:352), revealed some homology between the PRO1755 amino acid sequence and the following Dayhoff sequences: APG-BRANA, P_R37743, NAU88587_1, YHL1_EBV, P_W31855, CET10B10_4, AF039404_1, PRP1_HUMAN, AF038575_1, and AF053091_1.

Clone DNA76396-1698 was deposited with the ATCC on November 17, 1998, and is assigned ATCC deposit no. 203471.

EXAMPLE 106: Isolation of cDNA clones Encoding Human PRO1757

Use of the signal sequence algorithm described in Example 3 above allowed identification of three EST sequences from the Incyte database, designated Incyte EST clones no. 2007947, 2014962 and 1912034. These EST sequences were then clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated as DNA56054.

In light of the sequence homology between the DNA56054 sequence and a sequence contained within the Incyte EST clone no. 2007947, the Incyte EST clone no. 2007947 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 205 and is herein designated as DNA76398-1699.

Clone DNA76398-1699 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 59-61 and ending at the stop codon at nucleotide positions 422-424 (Figure 205). The

predicted polypeptide precursor is 121 amino acids long (Figure 206). The full-length PRO1757 protein shown in Figure 206 has an estimated molecular weight of about 12,073 daltons and a pI of about 4.11. Analysis of the full-length PRO1757 sequence shown in Figure 206 (SEQ ID NO:354) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, a transmembrane domain from about amino acid 91 to about amino acid 110, a glycosaminoglycan attachment site from about amino acid 44 to about amino acid 47, a cAMP- and cGMP-dependent protein kinase phosphorylation site from about amino acid 116 to about amino acid 119 and a potential N-myristoylation site from about amino acid 91 to about amino acid 96. Clone DNA76398-1699 has been deposited with ATCC on November 17, 1998 and is assigned ATCC deposit no. 203474.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 206 (SEQ ID NO:354), evidenced significant homology between the PRO1757 amino acid sequence and the following Dayhoff sequences: JQ0964, COLL_HSVS7, HSU70136_1, AF003473_1, D89728_1, MTF1_MOUSE, AF029777_1, HSU88153_1 and P_W05321.

15 EXAMPLE 107: Isolation of cDNA clones Encoding Human PRO1758

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated EST cluster No. 20926. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) from the databases mentioned above, to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56260.

In light of the sequence homology between the DNA56260 sequence and a sequence contained within EST no. 2936330 from the LIFESEQ® database, the EST clone, which originated from a library constructed from thymus tissue of a fetus that died from anencephalus, was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 207 and is herein designated as DNA76399-1700.

The full length clone shown in Figure 207 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 78 to 80 and ending at the stop codon found at nucleotide positions 549-551 (Figure 207; SEQ ID NO:355). The predicted polypeptide precursor (Figure 208, SEQ ID NO:356) is 157 amino acids long. PRO1758 has a calculated molecular weight of approximately 17,681 daltons and an estimated pI of approximately 7.65. Additional features include: a signal peptide from about amino acids 1-15; a potential N-glycosylation site at about amino acids 24-27; a cAMP- and cGMP-dependent protein kinase phosphorylation site at about amino acids 27-30; a casein kinase II phosphorylation site at about amino acids 60-63; potential N-myristoylation sites at about amino acids 17-22, 50-55, 129-134, and 133-138; a cell attachment sequence at about amino acids 153-155; and a cytochrome c family heme-binding site signature at about amino

acids 18-23.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 208 (SEQ ID NO:356), revealed significant homology between the PRO1758 amino acid sequence and Dayhoff sequence no AC005328_2. Homology was also found between the PRO1758 amino acid sequence and Dayhoff sequence no. CELC46F2_1.

- 5 Clone DNA76399-1700 was deposited with the ATCC on November 17, 1998 and is assigned ATCC deposit no. 203472.

EXAMPLE 108: Isolation of cDNA clones Encoding Human PRO1575

- 10 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as "DNA35699". Based on the DNA35699 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1575.

PCR primers (forward and reverse) were synthesized:

- 15 forward PCR primers: CCAGCAGTGCCCATACTCCATAGC (35699.f1; SEQ ID NO:359);
TGACGAGTGGGATACACTGC (35699.f2; SEQ ID NO:360)
reverse PCR primer: GCTCTACGGAACTTCTGCTGTGG (35699.r1; SEQ ID NO:361)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35699 sequence which had the following nucleotide sequence:

- 20 hybridization probe: ATTCCCAGGCGTGTGTCATTTGGGATCAGCACTGATTCTGAGGTTCTGACAC
(35699.p1; SEQ ID NO:362)

- 25 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1575 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human pancreatic tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1575 (designated herein as DNA76401-1683 [Figure 209, SEQ ID NO:357]; and the derived protein sequence for PRO1575.

- 30 The entire coding sequence of PRO1575 is shown in Figure 209 (SEQ ID NO:357). Clone DNA76401-1683 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 22-24 and an apparent stop codon at nucleotide positions 841-843. The predicted polypeptide precursor is 273 amino acids long. The full-length PRO1575 protein shown in Figure 210 has an estimated molecular weight of about 30,480 daltons and a pI of about 4.60. Additional features include: a signal peptide at about amino acids 1-20; a transmembrane domain at about amino acids 143-162; a potential N-glycosylation site at about amino acids 100-103; and potential N-myristoylation sites at about amino acids 84-89, 103-108, 154-159, and 201-206.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 210 (SEQ ID NO:358), revealed significant

homology between the PRO1575 amino acid sequence and Dayhoff sequence A12005_1. Homology was also revealed between the PRO1575 amino acid sequence and the following additional Dayhoff sequences: P_P80615; P_R25297; P_R51696; A47300; PDI_DROME; P_R49829; P_R63807; DMALPADAP_1; and DRZNF6_1.

Clone DNA76401-1683 was deposited with the ATCC on October 20, 1998, and is assigned ATCC deposit no. 203360.

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EXAMPLE 109: Isolation of cDNA clones Encoding Human PRO1787

A consensus DNA sequence was assembled relative to other EST sequences using phrap to form an assembly as described in Example 1 above. This consensus sequence is designated herein "DNA45123". Based on homology of DNA45123 to Incyte EST 3618549 identified in the assembly, as well as other discoveries and information provided herein, the clone including this EST was purchased and sequenced. DNA sequencing of the clone gave the full-length DNA sequence for PRO1787 and the derived protein sequence for PRO1787.

The entire coding sequence of PRO1787 is included in Figure 211 (SEQ ID NO:363). Clone DNA76510-2504 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 163-165 and an apparent stop codon at nucleotide positions 970-972 of SEQ ID NO:363. The approximate locations of the signal peptide, transmembrane domain, N-glycosylation sites, N-myristoylation sites and a kinase phosphorylation site are indicated in Figure 212. The predicted polypeptide precursor is 269 amino acids long. Clone DNA76510-2504 has been deposited with the ATCC and is assigned ATCC deposit no. 203477. The full-length PRO1787 protein shown in Figure 212 has an estimated molecular weight of about 29,082 daltons and a pI of about 9.02.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 212 (SEQ ID NO:364), revealed sequence identity between the PRO1787 amino acid sequence and the following Dayhoff sequences: MYP0_RAT, MYP0_HUMAN, MYP0_BOVIN, GEN12838, HSSCN2B2_1, AF007783_1, HSU90716_1, P_W42015, XLU43330_1 and AF060231_1.

25

EXAMPLE 110: Isolation of cDNA clones Encoding Human PRO1781

Initial DNA sequences referred to herein as DNA58070 and DNA56340 were identified using a yeast screen, in a human SK-Lu-1 adenocarcinoma cell line cDNA library that preferentially represents the 5' ends of the primary cDNA clones. These sequences were clustered and assembled into a consensus DNA sequence using the computer program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence is designated herein as "DNA59575".

Based on the DNA59575 consensus sequence, the following oligonucleotides, were synthesized for use as probes to isolate a clone of the full-length coding sequence for PRO1781 from a human fetal lung cDNA library: TGGAAAAGAAGTCTGGTCAGAAGGTTTAGG (SEQ ID NO:367), CATTTGGCTTCATTCTCCTGCTCTG (SEQ ID NO:368), AAAACCTCAGAACTCATTTCACACC (SEQ ID NO:369) and GTCTCACCATGGTTGCTCTTGCCAAATTGTGGGAAGCAGGG (SEQ ID NO:370).

The full length DNA76522-2500 clone shown in Figure 213 contained a single open reading frame with

an apparent translational initiation site at nucleotide positions 21 to 23 and ending at the stop codon found at nucleotide positions 1141-1143 (Figure 213; SEQ ID NO:365). The predicted polypeptide precursor (Figure 214, SEQ ID NO:366) is 373 amino acids long. PRO1781 has a calculated molecular weight of approximately 41,221 daltons and an estimated pI of approximately 8.54. Additional features include: a possible signal peptide at about amino acids 1-19; a transmembrane domain at about amino acids 39-60; a tyrosine phosphorylation site at about amino acids 228-236; potential N-myristoylation sites at about amino acids 16-21, 17-22, 43-48, 45-50, 47-52, 49-54, 53-58, 58-63, 59-64, 62-67, 126-131, and 142-147; amidation sites at about amino acids 22-25 and 280-283; and a prokaryotic membrane lipoprotein lipid attachment site at about amino acids 12-22.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 214 (SEQ ID NO:366), revealed some homology between the PRO1781 amino acid sequence and the following Dayhoff sequences: CEY4510D_5, AP000001_146, P_R10676, DAC_STRSQ, CEC40H5_5, P_R35204, KPU58495_1, KPN16781_1, AF010403_1, and AF056116_14.

Clone DNA76522-2500 was deposited with the ATCC on November 17, 1998, and is assigned ATCC deposit no. 203469.

EXAMPLE 111: Isolation of cDNA clones Encoding Human PRO1556

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated EST Cluster No. 103158, and also referred to herein as "DNA10398". This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and the LIFESEQ® database, to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56417.

In light of the sequence homology between the DNA56417 sequence and a sequence contained within Incyte EST no. 959332, EST no. 959332 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 215 and is herein designated as DNA76529-1666.

The full length clone shown in Figure 215 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 85 to 87 and ending at the stop codon found at nucleotide positions 892 to 894 (Figure 215; SEQ ID NO:371). The predicted polypeptide precursor (Figure 216, SEQ ID NO:372) is 269 amino acids long. PRO1556 has a calculated molecular weight of approximately 28,004 daltons and an estimated pI of approximately 5.80. Additional features include: a signal peptide sequence at about amino acids 1-24; transmembrane domains at about amino acids 11-25 and 226-243; a potential N-glycosylation site at about amino acids 182-185, potential cAMP- and cGMP-dependent protein kinase phosphorylation site at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 29-34, 35-39, 117-122, 121-126, 125-130, 154-159, 166-171, 241-246, 246-251, 247-252, 249-254, 250-255, 251-256,

252-257, 253-258, 254-259, 255-260, 256-261, 257-262, and 259-264.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 216 (SEQ ID NO:372), revealed some homology between the PRO1556 amino acid sequence and the following Dayhoff sequences: T8F5_4, R23B_MOUSE, CANS_HUMAN, P_W41640, DSU51091_1, TP2B_CHICK, DVU20660_1, S43296, P_R23962, and
5 BRN1_HUMAN.

Clone DNA76529-1666 was deposited with the ATCC on October 6, 1998, and is assigned ATCC deposit no. 203315.

EXAMPLE 112: Isolation of cDNA clones Encoding Human PRO1759

10 Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated DNA10571. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from pooled eosinophils of allergic asthmatic
15 patients. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57313.

20 In light of the sequence homology between the DNA57313 sequence and the Incyte EST 2434255, the clone including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 217 and is herein designated as DNA76531-1701.

The full length clone shown in Figure 217 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 125-127 and ending at the stop codon found at nucleotide
25 positions 1475-1477 (Figure 217; SEQ ID NO:373). The approximate locations of the signal peptide and transmembrane domains are indicated in Figure 218, whereas the approximate locations for N-myristoylation sites, a lipid attachment site, an amidation site and a kinase phosphorylation site are indicated in Figure 218. The predicted polypeptide precursor (Figure 218, SEQ ID NO:374) is 450 amino acids long. PRO1759 has a calculated molecular weight of approximately 49,765 daltons and an estimated pI of approximately 8.14. Clone
30 DNA76531-1701 was deposited with the ATCC on November 17, 1998 and is assigned ATCC deposit no. 203465.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 218 (SEQ ID NO:374), revealed sequence identity between the PRO1759 amino acid sequence and the following Dayhoff sequences: OPDE_PSEAE,
35 TH11_TRYBB, S67684, RGT2_YEAST, S68362, ATSUGTRPR_1, P_W17836 (Patent application WO9715668-A2), F69587, A48076, and A45611.

EXAMPLE 113: Isolation of cDNA clones Encoding Human PRO1760

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from a prostate tumor library. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA58798.

In light of the sequence homology between DNA58798 sequence and the Incyte EST 3358745, the clone including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 219 and is herein designated as DNA76532-1702.

The full length clone shown in Figure 219 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 60-62 and ending at the stop codon found at nucleotide positions 624-626 (Figure 219; SEQ ID NO:375). The predicted polypeptide precursor (Figure 220, SEQ ID NO:376) is 188 amino acids long. Motifs are further indicated in Figure 220. PRO1760 has a calculated molecular weight of approximately 21,042 daltons and an estimated pI of approximately 5.36. Clone DNA76532-1702 was deposited with the ATCC on November 17, 1998 and is assigned ATCC deposit no. 203473.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 220 (SEQ ID NO:376), revealed sequence identity between the PRO1760 amino acid sequence and the following Dayhoff sequences: CELT07F12_2, T22J18_16, ATF1C12_3, APE3_YEAST, P_W22471, SAU56908_1, SCPA_STRPY, ATAC00423817, SAPURCLUS_2 and AF041468_9.

EXAMPLE 114: Isolation of cDNA clones Encoding Human PRO1561

A consensus DNA sequence was assembled relative to other EST sequences using phrap and repeated cycles of BLAST and phrap to extend a sequence as far as possible using the EST sequences discussed above as described in Example 1 above. This consensus sequence is herein designated DNA40630. Based on the DNA40630 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1561.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (40630.f1) 5'-CTGCCTCCACTGCTCTGTGCTGGG-3' (SEQ ID NO:379)
reverse PCR primer (40630.r1) 5'-CAGAGCAGTGGATGTTCCCCTGGG-3' (SEQ ID NO:380)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40630 sequence which had the following nucleotide sequence

hybridization probe (40630.pl)

5'-CTGAACAAGATGGTCAAGCAAGTGACTGGGAAAATGCCCATCCTC-3' (SEQ ID NO:381)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1561 gene using the probe oligonucleotide and one of the PCR primers. RNA
5 for construction of the cDNA libraries was isolated from human breast tumor tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1561 (designated herein as DNA76538-1670 [Figure 221, SEQ ID NO:377]; and the derived protein sequence for PRO1561.

The entire nucleotide sequence of DNA76538-1670 is shown in Figure 221 (SEQ ID NO:377). Clone
10 DNA76538-1670 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 29-31 and ending at the stop codon at nucleotide positions 377-379 (Figure 221). The predicted polypeptide precursor is 116 amino acids long (Figure 222). The full-length PRO1561 protein shown in Figure 222 has an estimated molecular weight of about 12,910 daltons and a pI of about 6.41. Analysis of the full-length PRO1561 sequence shown in Figure 222 (SEQ ID NO:378) evidences the presence of the following:
15 a signal peptide from about amino acid 1 to about amino acid 17, a transmembrane domain from about amino acid 1 to about amino acid 24, a potential N-glycosylation site from about amino acid 86 to about amino acid 89, potential N-myristoylation sites from about amino acid 20 to about amino acid 25 and from about amino acid 45 to about amino acid 50 and a phospholipase A2 histidine active site from about amino acid 63 to about amino acid 70. Clone DNA76538-1670 has been deposited with ATCC on October 6, 1998 and is assigned ATCC
20 deposit no. 203313.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 222 (SEQ ID NO:378), evidenced significant homology between the PRO1561 amino acid sequence and the following Dayhoff sequences: P_R63053, P_R25416, P_R63055, P_P93363, P_R63046, PA2A_VIPAA, P_W58476, GEN13747, PA2X_HUMAN and
25 PA2A_CRODU.

In addition to the above, a sequence homology search evidenced significant homology between the DNA40630 consensus sequence and Incyte EST clone no. 1921092. As such, Incyte EST clone no. 1921092 was purchased and the insert obtained and sequenced, thereby giving rise to the DNA76538-1670 sequence shown in Figure 221 (SEQ ID NO:377).
30

EXAMPLE 115: Isolation of cDNA clones Encoding Human PRO1567

A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated DNA47580. The DNA47580 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database
35 (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater

that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated "DNA57246".

In light of the sequence homology between the DNA57246 sequence and EST no. 1793996 from the LIFESEQ™ database, the clone containing the EST no. 1793996, which originates from a library constructed from prostate tumor tissue, was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 223 (SEQ ID NO:382) and is herein designated as DNA76541-1675.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 109-111, and a stop signal at nucleotide positions 643-645 (Fig. 223; SEQ ID NO:382). The predicted polypeptide precursor is 178 amino acids long has a calculated molecular weight of approximately 19,600 daltons and an estimated pI of approximately 5.89. Additional features include a signal peptide at about amino acids 1-22; a potential N-glycosylation site at about amino acids 167-170; a protein kinase C phosphorylation site at about amino acids 107-109; and potential N-myristoylation sites at about amino acids 46-51, 72-77, and 120-125.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 224 (SEQ ID NO:383), evidenced significant homology between the PRO1567 amino acid sequence and human colon specific gene CSG6 polypeptide designated Dayhoff sequence "P_W06549". Homology was also found between the PRO1567 amino acid sequence and the following additional Dayhoff sequences: HUAC002301_1, P_246880, A49685, SPBP_RAT, S42924, SPBP_MOUSE, I52115, MMU03711_1, and AF041468_31.

Clone DNA76541-1675 has been deposited with the ATCC on October 27, 1998, and is assigned ATCC deposit no. 203409.

EXAMPLE 116: Isolation of cDNA clones Encoding Human PRO1693

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA38251. Based on the DNA38251 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1693.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (38251.f1) 5'-CTGGGATCTGAACAGTTTCGGGGC-3' (SEQ ID NO:386)

reverse PCR primer (38251.r1) 5'-GGTCCCCAGGACATGGTCTGTCCC-3' (SEQ ID NO:387)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA38251 sequence which had the following nucleotide sequence

hybridization probe (38251.p1)

5'-GCTGAGTTTACATTTACGGTCTAACTCCCTGAGAACCATCCCTGTGCG-3' (SEQ ID NO:388)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to

isolate clones encoding the PRO1693 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1693 (designated herein as DNA77301-1708 [Figure 225, SEQ ID NO:384]; and the derived protein sequence for PRO1693.

5 The entire nucleotide sequence of DNA77301-1708 is shown in Figure 225 (SEQ ID NO:384). Clone DNA77301-1708 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 508-510 and ending at the stop codon at nucleotide positions 2047-2049 (Figure 225). The predicted polypeptide precursor is 513 amino acids long (Figure 226). The full-length PRO1693 protein shown in Figure 226 has an estimated molecular weight of about 58,266 daltons and a pI of about 9.84. Analysis of the full-length PRO1693 sequence shown in Figure 226 (SEQ ID NO:385) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 33, a transmembrane domain from about amino acid 420 to about amino acid 442, potential N-glycosylation sites from about amino acid 126 to about amino acid 129, from about amino acid 357 to about amino acid 360, from about amino acid 496 to about amino acid 499 and from about amino acid 504 to about amino acid 507, a cAMP- and cGMP-dependent protein kinase phosphorylation site from about amino acid 465 to about amino acid 468, a tyrosine kinase phosphorylation site from about amino acid 136 to about amino acid 142 and potential N-myristoylation sites from about amino acid 11 to about amino acid 16, from about amino acid 33 to about amino acid 38, from about amino acid 245 to about amino acid 250, from about amino acid 332 to about amino acid 337, from about amino acid 497 to about amino acid 502 and from about amino acid 507 to about amino acid 512. Clone DNA77301-1708 has been deposited with ATCC on October 27, 1998 and is assigned ATCC deposit no. 203407.

15 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 226 (SEQ ID NO:385), evidenced significant homology between the PRO1693 amino acid sequence and the following Dayhoff sequences: AB007876_1, ALS_MOUSE, HSCHON03_1, P_R85889, AF062006_1, AB014462_1, A58532, MUSLRRPA_1, AB007865_1 and AF030435_1.

EXAMPLE 117: Isolation of cDNA clones Encoding Human PRO1784

A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated DNA43862. Based on the DNA43862 sequence, oligonucleotide probes were generated and used to screen a human fetal kidney library prepared as described in paragraph 1 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and reverse) were synthesized:

35 forward PCR primer (f1) 5'-CTTTTCAGTGTCACCTCAGCGATCTC-3' (SEQ ID NO:391); and
 reverse PCR primer (r1) 5'-CCAAAACATGGAGCAGGAACAGG-3' (SEQ ID NO:392).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA43862 sequence which had the following nucleotide sequence:

hybridization probe (p1)

5'-CCAGTTGGTGCTCTCGGACCTACCATGCGAAGAAGATGAAATGTGTG-3' (SEQ ID NO:393).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1784 gene using the probe oligonucleotide and one of the PCR primers.

- 5 A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 68-70, and a stop signal at nucleotide positions 506-508 (Fig. 227; SEQ ID NO:389). The predicted polypeptide precursor is 146 amino acids long has a calculated molecular weight of approximately 16,116 daltons and an estimated pI of approximately 4.99. The approximate locations of the signal peptide, transmembrane domain and N-myristoylation site are indicated in Figure 228. Clone
10 DNA77303-2502 has been deposited with the ATCC and is assigned ATCC deposit no. 203479.

- An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 228 (SEQ ID NO:390), evidenced sequence identity between the PRO1784 amino acid sequence and the following Dayhoff sequences: RNU87224_1, RNAF000114_1, P_W31947, S18038, AE001300_8, AF039833_1, P_W39833_1, P_W39788, HSU87223_1,
15 NTU06712_1, and P_W31946.

EXAMPLE 118: Isolation of cDNA clones Encoding Human PRO1605

- A cDNA clone (DNA77648-1688) encoding a native human PRO1605 polypeptide was identified by a yeast screen, in a human fetal kidney cDNA library that preferentially represents the 5' ends of the primary
20 cDNA clones.

- The full-length DNA77648-1688 clone shown in Figure 229 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 425-427 and ending at the stop codon at nucleotide positions 845-847 (Figure 229). The predicted polypeptide precursor is 140 amino acids long (Figure 230). The full-length PRO1605 protein shown in Figure 230 has an estimated molecular weight of about 15,668 daltons
25 and a pI of about 10.14. Analysis of the full-length PRO1605 sequence shown in Figure 230 (SEQ ID NO:395) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 26. Clone DNA77648-1688 has been deposited with ATCC on October 27, 1998 and is assigned ATCC deposit no. 203408.

- An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence
30 alignment analysis of the full-length sequence shown in Figure 230 (SEQ ID NO:395), evidenced significant homology between the PRO1605 amino acid sequence and the following Dayhoff sequences: GNT5_HUMAN, P_R48975, P_W22519, MM26SPROT_1, HSU86782_1, CH60_LEPIN, HMCT_HELPY, F65126, HIU08875_1 and P_R41724.

- 35 EXAMPLE 119: Isolation of cDNA clones Encoding Human PRO1788

The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about 950 known secreted proteins from the Swiss-Prot public database were used to search EST databases. The EST

databases included public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)] as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Incyte Clone No. 2968304 was identified as a sequence of interest having a BLAST score of 70 or greater that did not encode known proteins. The nucleotide sequence of Incyte Clone No. 2968304 is designated herein as "DNA6612".

In addition, the DNA6612 sequence was extended using repeated cycles of BLAST and phrap (Phil Green, University of Washington, Seattle, Washington) to extend the sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is designated herein as "DNA49648". Based on the DNA49648 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1788.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: CCCTGCCAGCCGAGAGCTTCACC (49648.f1; SEQ ID NO:398)

reverse PCR primer: GGTTGGTGCCCGAAAGGTCCAGC (49648.r1; SEQ ID NO:399)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA49648 sequence which had the following nucleotide sequence:

hybridization probe: CAACCCCAAGCTTAACTGGGCAGGAGCTGAGGTGTTTTTCAGGCQ49648.p1; SEQ ID NO:400)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1788 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1788 (designated herein as DNA77652-2505 [Figure 231, SEQ ID NO:396]; and the derived protein sequence for PRO1788.

The entire coding sequence of PRO1788 is shown in Figure 231 (SEQ ID NO:396). Clone DNA77652-2505 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 64-66 and an apparent stop codon at nucleotide positions 1123-1125. The predicted polypeptide precursor is 353 amino acids long. The full-length PRO1788 protein shown in Figure 232 has an estimated molecular weight of about 37,847 daltons and a pI of about 6.80. Additional features of PRO1788 include: a signal peptide at about amino acids 1-16; transmembrane domains at about amino acids 215-232 and 287-304; potential N-glycosylation sites at about amino acids 74-77 and 137-140; a glycosaminoglycan attachment site at about amino acids 45-48; a tyrosine kinase phosphorylation site at about amino acids 318-325; N-myristoylation sites at about amino acids 13-18, 32-37, 88-93, 214-219, and 223-228; and a leucine zipper pattern at about amino acids 284-305.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 232 (SEQ ID NO:397), revealed significant homology between the PRO1788 amino acid sequence and the following Dayhoff sequences: AF030435_1;

AF062006_1; DMTARTAN_1; GARP_HUMAN; S42799; P_R71294; HSU88879_1; DROWHEELER_1; A58532; and AF068920_1.

Clone DNA77652-2505 was deposited with the ATCC on November 17, 1998, and is assigned ATCC deposit no. 203480.

5 EXAMPLE 120: Isolation of cDNA clones Encoding Human PRO1801

A proprietary expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed homology to the IL-19 protein. This EST sequence is Incyte EST clone no. 819592 and is herein designated DNA79293. Based on the DNA79293 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence
10 of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1801.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTCCTGTGGTCTCCAGATTTTCAGGCCTA-3' (SEQ ID NO:403)

reverse PCR primer 5'-AGTCCTCCTTAAGATTCTGATGTCAA-3' (SEQ ID NO:404)

RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue. The cDNA
15 libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280
20 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1801 (designated herein as DNA83500-2506 [Figure 233, SEQ ID NO:401]; and the derived protein sequence for PRO1801.

The entire nucleotide sequence of DNA83500-2506 is shown in Figure 233 (SEQ ID NO:401). Clone
25 DNA83500-2506 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 109-111 and ending at the stop codon at nucleotide positions 892-894 (Figure 233). The predicted polypeptide precursor is 261 amino acids long (Figure 234). The full-length PRO1801 protein shown in Figure 234 has an estimated molecular weight of about 29,667 daltons and a pI of about 8.76. Analysis of the full-length PRO1801 sequence shown in Figure 234 (SEQ ID NO:402) evidences the presence of the following: a
30 signal peptide from about amino acid 1 to about amino acid 42, cAMP- and cGMP-dependent protein kinase phosphorylation sites from about amino acid 192 to about amino acid 195 and from about amino acid 225 to about amino acid 228 and potential N-myristylation sites from about amino acid 42 to about amino acid 47, from about amino acid 46 to about amino acid 51 and from about amino acid 136 to about amino acid 141. Clone DNA83500-2506 has been deposited with ATCC on October 29, 1998 and is assigned ATCC deposit no.
35 203391.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 234 (SEQ ID NO:402), evidenced significant

homology between the PRO1801 amino acid sequence and the following Dayhoff sequences: P_W37935, HGS_B477, P_R32277, IL10_MACFA, P_W46585, P_R39714, P_R71471, P_R10159, IL10_RAT and P_W57201.

EXAMPLE 121: Isolation of cDNA clones Encoding Human UCP4

5 EST databases, which included public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA), were searched for sequences having homologies to human UCP3. The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the UCP3 protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater
10 that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program AssemblIGN and MacVector (Oxford Molecular Group, Inc.).

A DNA sequence ("fromDNA") was assembled relative to other EST sequences using AssemblIGN software. In addition, the fromDNA sequence was extended using repeated cycles of BLAST and AssemblIGN to extend the sequence as far as possible using the sources of EST sequences discussed above. Based on this
15 DNA sequence, oligonucleotides were synthesized to isolate a clone of the full-length coding sequences for UCP4 by PCR. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp.

20 PCR primers (forward and reverse) were synthesized:

forward PCR primer CGCGGATCCCGTTATCGTCTTGCGCTACTGC (SEQ ID NO:407)

reverse PCR primer GCGGAATTCTTAAAATGGACTGACTCCACTCATC (SEQ ID NO:408)

RNA for construction of the cDNA libraries was isolated from brain tissue. The cDNA libraries used to isolated the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked
25 with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

30 DNA sequencing of the clone isolated by PCR as described above gave the full-length DNA sequence for UCP4 (designated herein as DNA77568-1626 [Figure 235, SEQ ID NO:405] and the derived protein sequence for UCP4.

The entire coding sequence of UCP4 is shown in Figure 235 (SEQ ID NO:405). Clone DNA77568-1626 contains a single open reading frame with an apparent translational initiation site at nucleotide positions
35 27-29, and an apparent stop codon at nucleotide positions 996-998. (See Figure 235; SEQ ID NO:405). The predicted polypeptide precursor is 323 amino acids long. It is presently believed that UCP4 is a membrane-bound protein and contains at least 6 transmembrane regions. These putative transmembrane regions in the

UCP4 amino acid sequence are illustrated in Figure 236. Clone DNA77568-1626, contained in the pcDNA3 vector (Invitrogen) has been deposited with ATCC and is assigned ATCC deposit no. 203134. UCP4 polypeptide is obtained or obtainable by expressing the molecule encoded by the cDNA insert of the deposited ATCC 203134 vector. Digestion of the vector with BamHI and EcoRI restriction enzymes will yield an approximate 972 plus 34 bp insert. The full-length UCP4 protein shown in Figure 236 has an estimated
5 molecular weight of about 36,061 daltons and a pI of about 9.28.

EXAMPLE 122: Isolation of cDNA clones Encoding Human PRO193

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. Based on this consensus sequence, oligonucleotides were synthesized: 1) to identify by
10 PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO193.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GTTTGAGGAAGCTGGGATAC-3' (SEQ ID NO:411); and

reverse PCR primer 5'-CCAAACTCGAGCACCTGTTC-3' (SEQ ID NO:412).

15 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus sequence which had the following nucleotide sequence:

hybridization probe

5'-ATGGCAGGCTTCCTAGATAATTTTCGTTGGCCAGAATGTG-3' (SEQ ID NO:413).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was
20 screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO193 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human retina tissue (LIB94).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO193 [herein designated as DNA23322-1393] (SEQ ID NO:409) and the derived protein sequence for
25 PRO193.

The entire nucleotide sequence of DNA23322-1393 is shown in Figure 237 (SEQ ID NO:409). Clone DNA23322-1393 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 138-140 and ending at the stop codon at nucleotide positions 612-614 (Figure 237). The predicted polypeptide precursor is 158 amino acids long (Figure 238). The full-length PRO193 protein shown in Figure
30 238 has an estimated molecular weight of about 17,936 and a pI of about 5.32. Clone DNA23322-1393 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Still analyzing the amino acid sequence of SEQ ID NO:410, transmembrane domains are at about amino acids 23-42, 60-80, 97-117 and 128-148 of SEQ ID NO:410. A cell attachment sequence is at about amino acids
35 81-83 of SEQ ID NO:410. A peroxidase proximal heme-ligand domain is at about amino acids 81-83 of SEQ ID NO:410. The corresponding nucleotides can be routinely determined given the sequences provided herein.

EXAMPLE 123: Isolation of cDNA clones Encoding Human PRO1130

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA34360. Based on the DNA34360 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for

5 PRO1130.

PCR primers (forward and reverse) were synthesized:

- forward PCR primer (34360.f1) 5'-GCCATAGTCACGACATGGATG-3' (SEQ ID NO:416)
- forward PCR primer (34360.f2) 5'-GGATGGCCAGAGCTGCTG-3' (SEQ ID NO:417)
- forward PCR primer (34360.f3) 5'-AAAGTACAAGTGTGGCCTCATCAAGC-3' (SEQ ID NO:418)
- 10 reverse PCR primer (34360.r1) 5'-TCTGACTCCTAAGTCAGGCAGGAG-3' (SEQ ID NO:419)
- reverse PCR primer (34360.r2) 5'-ATTCTCTCCACAGACAGCTGGTTC-3' (SEQ ID NO:420)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA34360 sequence which had the following nucleotide sequence

- hybridization probe (34360.p1)
- 15 5'-GTACAAGTGTGGCCTCATCAAGCCCTGCCCAGCCAACTACTTTGCG-3' (SEQ ID NO:421)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1130 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human aortic endothelial cell tissue.

- 20 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1130 (designated herein as DNA59814-1486 [Figure 239, SEQ ID NO:414]; and the derived protein sequence for PRO1130.

- The entire nucleotide sequence of DNA59814-1486 is shown in Figure 239 (SEQ ID NO:414). Clone DNA59814-1486 contains a single open reading frame with an apparent translational initiation site at nucleotide
- 25 positions 312-314 and ending at the stop codon at nucleotide positions 984-986 (Figure 239). The predicted polypeptide precursor is 224 amino acids long (Figure 240). The full-length PRO1130 protein shown in Figure 240 has an estimated molecular weight of about 24,963 daltons and a pI of about 9.64. Analysis of the full-length PRO1130 sequence shown in Figure 240 (SEQ ID NO:415) evidences the presence of the following: a
- 30 signal peptide from about amino acid 1 to about amino acid 15, an ATP/GTP-binding site motif A from about amino acid 184 to about amino acid 191 and a potential N-glycosylation site from about amino acid 107 to about amino acid 110. Clone DNA59814-1486 has been deposited with ATCC on October 20, 1998 and is assigned ATCC deposit no. 203359.

- An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 240 (SEQ ID NO:415), evidenced significant
- 35 homology between the PRO1130 amino acid sequence and the following Dayhoff sequences: P_W06547, 216_HUMAN, D87120_1, MMU72677_1, LAU04889_1, and D69319.

EXAMPLE 124: Isolation of cDNA clones Encoding Human PRO1335

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA35727. Based on the DNA35727 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1335.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (35727.f1) 5'-GTAAAGTCGCTGGCCAGC-3' (SEQ ID NO:424)

forward PCR primer (35727.f2) 5'-CCCGATCTGCCTGCTGTA-3' (SEQ ID NO:425)

reverse PCR primer (35727.r1) 5'-CTGCACTGTATGGCCATTATTGTG-3' (SEQ ID NO:426)

10 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35727 sequence which had the following nucleotide sequence

hybridization probe (35727.pl)

5'-CAGAAACCCATGATACCCTACTGAACACCGAATCCCCTGGAAGCC-3' (SEQ ID NO:427)

15 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1335 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human retina tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1335 (designated herein as DNA62812-1594 [Figure 241, SEQ ID NO:422]; and the derived protein sequence for PRO1335.

20 The entire nucleotide sequence of DNA62812-1594 is shown in Figure 241 (SEQ ID NO:422). Clone DNA62812-1594 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 271-273 and ending at the stop codon at nucleotide positions 1282-1284 (Figure 241). The predicted polypeptide precursor is 337 amino acids long (Figure 242). The full-length PRO1335 protein shown in Figure 242 has an estimated molecular weight of about 37,668 daltons and a pI of about 6.27. Analysis of the full-length PRO1335 sequence shown in Figure 242 (SEQ ID NO:423) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15, a transmembrane domain from about amino acid 291 to about amino acid 310, a potential N-glycosylation site from about amino acid 213 to about amino acid 216 and amino acid sequence blocks having homology to eukaryotic-type carbonic anhydrase proteins from about amino acid 197 to about amino acid 245, from about amino acid 104 to about amino acid 140 and from about amino acid 22 to about amino acid 69. Clone DNA62812-1594 has been deposited with ATCC on September 9, 1998 and is assigned ATCC deposit no. 203248.

35 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 242 (SEQ ID NO:423), evidenced significant homology between the PRO1335 amino acid sequence and the following Dayhoff sequences: AF037335_1, I38013, PTPG_MOUSE, CAH2_HUMAN, ICAC, CAH7_HUMAN, CAH3_HUMAN, CAH1_HUMAN, CAH5_HUMAN and P_R41746.

EXAMPLE 125: Isolation of cDNA clones Encoding Human PRO1329

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte Cluster No. 167544, also referred herein as "DNA10680". This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs was derived from a cDNA library constructed from RNA isolated from synovial membrane tissue removed from the elbow of a female with rheumatoid arthritis. The consensus sequence obtained therefrom is herein designated "DNA58836".

In light of the sequence homology between the DNA58836 sequence and a sequence contained within the Incyte EST clone no. 368774, EST clone 368774 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 243 and is herein designated as DNA66660-1585.

The full length clone shown in Figure 243 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 90 to 92 and ending at the stop codon found at nucleotide positions 717 to 719 (Figure 243; SEQ ID NO:428). The predicted polypeptide precursor (Figure 244, SEQ ID NO:429) is 209 amino acids long, with a signal sequence at about amino acids 1-16. PRO1329 has a calculated molecular weight of approximately 21,588 daltons and an estimated pI of approximately 5.50. Clone DNA66660-1585 was deposited with the ATCC on September 22, 1998 and is assigned ATCC deposit no. 203279.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 244 (SEQ ID NO:429), revealed some homology between the PRO1329 amino acid sequence and the following Dayhoff sequences: CELK06A9_3, PROA_XANCP, CXU21300_4, MTV037_17, SYN1_RAT, I56542, S60743, BNOLE3_1, AB001573_1, and P_P80671.

EXAMPLE 126: Isolation of cDNA clones Encoding Human PRO1550

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST sequence from the Merck database, designated CELT15B7_12, also referred herein as "DNA10022". This EST sequence was then compared to a variety of expressed sequence tag (EST) databases which included public and proprietary EST databases (e.g., GenBank and LIFESEQ®) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the

program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated "DNA55708".

In light of the sequence homology between the DNA55708 sequence and a sequence contained within Incyte EST no. 3411659, the EST clone 3411659 was purchased and the cDNA insert was obtained and sequenced in its entirety. The sequence of this cDNA insert is shown in Figure 245 and is herein designated as
5 "DNA76393-1664".

The full length clone shown in Figure 245 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 138 to 140 and ending at the stop codon found at nucleotide positions 867 to 869 (Figure 245; SEQ ID NO:430). The predicted polypeptide precursor (Figure 246, SEQ ID NO:431) is 243 amino acids long. Other features of the PRO1550 protein include: a signal sequence at about
10 amino acids 1-30; a hydrophobic domain at about amino acids 195-217; and a potential N-glycosylation site at about amino acids 186-189. PRO1550 has a calculated molecular weight of approximately 26,266 daltons and an estimated pI of approximately 8.43. Clone DNA76393-1664 was deposited with the ATCC on October 6, 1998, and is assigned ATCC deposit no. 203323.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence
15 alignment analysis of the full-length sequence shown in Figure 246 (SEQ ID NO:431), revealed some homology between the PRO1550 amino acid sequence and the following Dayhoff sequences: CELF59E12_11; CA24_ASCSU; AF018082_1; CA13_BOVIN; CA54_HUMAN; CA34_HUMAN; HUMCOL7AIX_1; P_W09643; AF053538_1; and HSEM CXIV2_1.

20 EXAMPLE 127: Use of PRO as a hybridization probe

The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe.

DNA comprising the coding sequence of full-length or mature PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in human tissue cDNA libraries or human tissue genomic libraries.

25 Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

30 DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

EXAMPLE 128: Expression of PRO in *E. coli*

This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in
35 *E. coli*.

The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected

expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from *E. coli*; see Bolivar et al., Gene, 2:95 (1977)) which contains genes for ampicillin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis
5 sequence, and enterokinase cleavage site), the PRO coding region, lambda transcriptional terminator, and an argU gene.

The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., supra. Transformants are identified by their ability to grow on LB plates and antibiotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA
10 sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell
15 pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the protein.

PRO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding PRO is initially amplified using selected PCR primers. The primers will contain restriction enzyme
20 sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) lon galE rpoHts(htpRts) clpP(lacIq). Transformants are first grown in LB containing 50 mg/ml
25 carbenicillin at 30°C with shaking until an O.D.600 of 3-5 is reached. Cultures are then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g (NH₄)₂SO₄, 0.71 g sodium citrate•2H₂O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55 % (w/v) glucose and 7 mM MgSO₄) and grown for approximately 20-30 hours at 30°C with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell
30 pellets are frozen until purification and refolding.

E. coli paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000
35 rpm in a Beckman Ultracentrifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate

column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

5 The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4°C for 12-36 hours. The refolding reaction is quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The
10 refolded protein is chromatographed on a Poros R1/H reversed phase column using a mobile buffer of 0.1% TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the
15 reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin from the samples.

Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with
20 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 129: Expression of PRO in mammalian cells

25 This example illustrates preparation of a potentially glycosylated form of PRO by recombinant expression in mammalian cells.

The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector. Optionally, the PRO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO DNA using ligation methods such as described in Sambrook et al., supra. The resulting vector is called pRK5-
30 PRO.

In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10 µg pRK5-PRO DNA is mixed with about 1 µg DNA encoding the VA RNA gene [Thimmappaya et al., Cell, 31:543 (1982)] and dissolved in 500 µl of 1 mM
35 Tris-HCl, 0.1 mM EDTA, 0.227 M CaCl₂. To this mixture is added, dropwise, 500 µl of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM NaPO₄, and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The

culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200 $\mu\text{Ci/ml}$ ^{35}S -cysteine and 200 $\mu\text{Ci/ml}$ ^{35}S -methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Sompanyrac et al., Proc. Natl. Acad. Sci., 12:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700 μg pRK5-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5 $\mu\text{g/ml}$ bovine insulin and 0.1 $\mu\text{g/ml}$ bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as CaPO_4 or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as ^{35}S -methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a poly-his tag into a Baculovirus expression vector. The poly-his tagged PRO insert can then be subcloned into a SV40 driven vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged PRO can then be concentrated and purified by any selected method, such as by Ni^{2+} -chelate affinity chromatography.

PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using

standard techniques as described in Ausubel et al., Current Protocols of Molecular Biology, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., Nucl. Acids Res. 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transfection.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect* (Quiagen), Dosper* or Fugene* (Boehringer Mannheim). The cells are grown as described in Lucas et al., supra. Approximately 3×10^7 cells are frozen in an ampule for further growth and production as described below.

The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mLs of media and centrifuged at 1000 rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2 μ m filtered PS20 with 5% 0.2 μ m diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 250 mL spinner filled with 150 mL selective growth medium and incubated at 37°C. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with 3×10^5 cells/mL. The cell media is exchanged with fresh media by centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Patent No. 5,122,469, issued June 16, 1992 may actually be used. A 3L production spinner is seeded at 1.2×10^6 cells/mL. On day 0, the cell number pH is determined. On day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22 μ m filter. The filtrate was either stored at 4°C or immediately loaded onto columns for purification.

For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4°C. After loading, the column is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C.

Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275 μ L of 1 M Tris buffer, pH 9. The highly purified protein is subsequently

desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 130: Expression of PRO in Yeast

5 The following method describes recombinant expression of PRO in yeast.

First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding PRO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO
10 signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of PRO.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with
15 Coomassie Blue stain.

Recombinant PRO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing PRO may further be purified using selected column chromatography resins.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.
20

EXAMPLE 131: Expression of PRO in Baculovirus-Infected Insect Cells

The following method describes recombinant expression of PRO in Baculovirus-infected insect cells.

The sequence coding for PRO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG).
25 A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product
30 is then digested with those selected restriction enzymes and subcloned into the expression vector.

Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold™ virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., Baculovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).
35

Expressed poly-his tagged PRO can then be purified, for example, by Ni²⁺-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by

Rupert et al., *Nature*, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl₂; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 μ m filter. A Ni²⁺-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A₂₈₀ with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound protein. After reaching A₂₈₀ baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with Ni²⁺-NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His₁₀-tagged PRO are pooled and dialyzed against loading buffer.

Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 132: Preparation of Antibodies that Bind PRO

This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.

Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, *supra*. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against PRO is within the skill in the art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

5

EXAMPLE 133: Purification of PRO Polypeptides Using Specific Antibodies

Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSE™ (Pharmacia LKB Biotechnology). The antibody is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's instructions.

Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (*e.g.*, high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (*e.g.*, a low pH buffer such as approximately pH 2-3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

30 EXAMPLE 134: Drug Screening

This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO

polypeptide or a fragment and the agent being tested. Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with an PRO polypeptide or fragment thereof and assaying (i) for the presence of a complex between the agent and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with PRO polypeptide.

EXAMPLE 135: Rational Drug Design

The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (*i.e.*, a PRO polypeptide) or of small molecules with which they interact, *e.g.*, agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide *in vivo* (*c.f.*, Hodgson, Bio/Technology, 9: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of an PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, Biochemistry, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda *et al.*, J. Biochem., 113:742-746

(1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced peptides. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to x-ray crystallography.

Deposit of Material

The following materials have been deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209, USA (ATCC):

Table 2

<u>Material</u>	<u>ATCC Dep. No.</u>	<u>Deposit Date</u>
DNA19902-1669	203454	November 3, 1998
20 DNA26846-1397	203406	October 27, 1998
DNA56107-1415	203405	October 27, 1998
DNA56406-1704	203478	November 17, 1998
DNA56529-1647	203293	September 29, 1998
DNA56531-1648	203286	September 29, 1998
25 DNA56862-1343	203174	September 1, 1998
DNA57254-1477	203289	September 29, 1998
DNA57841-1522	203458	November 3, 1998
DNA58727-1474	203171	September 1, 1998
DNA58730-1607	203221	September 15, 1998
30 DNA58732-1650	203290	September 29, 1998
DNA58828-1519	203172	September 1, 1998
DNA58852-1637	203271	September 22, 1998
DNA59212-1627	203245	September 9, 1998
DNA59218-1559	203287	September 29, 1998
35 DNA59219-1613	203220	September 15, 1998
DNA59586-1520	203288	September 29, 1998
DNA59817-1703	203470	November 17, 1998
DNA60278-1530	203170	September 1, 1998
DNA60608-1577	203126	August 18, 1998
40 DNA60611-1524	203175	September 1, 1998
DNA60618-1557	203292	September 29, 1998
DNA60740-1615	203456	November 3, 1998
DNA60764-1533	203452	November 10, 1998
DNA60775-1532	203173	September 1, 1998
45 DNA61185-1646	203464	November 17, 1998
DNA61608-1606	203239	September 9, 1998
DNA62808-1326	203358	October 20, 1998

	DNA62809-1531	203237	September 9, 1998
	DNA62815-1578	203247	September 9, 1998
	DNA62845-1684	203361	October 20, 1998
	DNA64842-1632	203278	September 22, 1998
	DNA64849-1604	203468	November 17, 1998
5	DNA64863-1573	203251	September 9, 1998
	DNA64881-1602	203240	September 9, 1998
	DNA64883-1526	203253	September 9, 1998
	DNA64885-1529	203457	November 3, 1998
	DNA64886-1601	203241	September 9, 1998
10	DNA64888-1542	203249	September 9, 1998
	DNA64889-1541	203250	September 9, 1998
	DNA64897-1628	203216	September 15, 1998
	DNA64902-1667	203317	October 6, 1998
	DNA64903-1553	203223	September 15, 1998
15	DNA64905-1558	203233	September 15, 1998
	DNA64950-1590	203224	September 15, 1998
	DNA64952-1568	203222	September 15, 1998
	DNA65402-1540	203252	September 9, 1998
	DNA65403-1565	203230	September 15, 1998
20	DNA65404-1551	203244	September 9, 1998
	DNA65405-1547	203476	November 17, 1998
	DNA65406-1567	203219	September 15, 1998
	DNA65408-1578	203217	September 15, 1998
	DNA65409-1566	203232	September 15, 1998
25	DNA65410-1569	203231	September 15, 1998
	DNA65423-1595	203227	September 15, 1998
	DNA66304-1546	203321	October 6, 1998
	DNA66511-1411	203228	September 15, 1998
	DNA66512-1564	203218	September 15, 1998
30	DNA66519-1535	203236	September 15, 1998
	DNA66520-1536	203226	September 15, 1998
	DNA66521-1583	203225	September 15, 1998
	DNA66526-1616	203246	September 9, 1998
	DNA66658-1584	203229	September 15, 1998
35	DNA66659-1593	203269	September 22, 1998
	DNA66663-1598	203268	September 22, 1998
	DNA66669-1597	203272	September 22, 1998
	DNA66672-1586	203265	September 22, 1998
	DNA66674-1599	203281	September 22, 1998
40	DNA66675-1587	203282	September 22, 1998
	DNA67962-1649	203291	September 29, 1998
	DNA68836-1656	203455	November 3, 1998
	DNA68864-1629	203276	September 22, 1998
	DNA68866-1644	203283	September 22, 1998
45	DNA68871-1638	203280	September 22, 1998
	DNA68874-1622	203277	September 22, 1998
	DNA68880-1676	203319	October 6, 1998
	DNA68885-1570	203311	October 6, 1998
	DNA71166-1685	203355	October 20, 1998
50	DNA71169-1709	203467	November 17, 1998
	DNA71180-1655	203403	October 27, 1998
	DNA71184-1634	203266	September 22, 1998
	DNA71213-1659	203401	October 27, 1998
	DNA71234-1651	203402	October 27, 1998
55	DNA71277-1636	203285	September 22, 1998
	DNA71282-1668	203312	October 6, 1998

	DNA71286-1604	203357	October 20, 1998
	DNA71883-1660	203475	November 17, 1998
	DNA73401-1633	203273	September 22, 1998
	DNA73492-1671	203324	October 6, 1998
	DNA73727-1673	203459	November 3, 1998
5	DNA73730-1679	203320	October 6, 1998
	DNA73734-1680	203363	October 20, 1998
	DNA73735-1681	203356	October 20, 1998
	DNA73736-1657	203466	November 17, 1998
	DNA73737-1658	203412	October 27, 1998
10	DNA73739-1645	203270	September 22, 1998
	DNA73742-1662	203316	October 6, 1998
	DNA73744-1665	203322	October 6, 1998
	DNA73746-1654	203411	October 27, 1998
	DNA73760-1672	203314	October 6, 1998
15	DNA76396-1698	203471	November 17, 1998
	DNA76398-1699	203474	November 17, 1998
	DNA76399-1700	203472	November 17, 1998
	DNA76401-1683	203360	October 20, 1998
	DNA76510-2504	203477	November 17, 1998
20	DNA76522-2500	203469	November 17, 1998
	DNA76529-1666	203315	October 6, 1998
	DNA76531-1701	203465	November 17, 1998
	DNA76532-1702	203473	November 17, 1998
	DNA76538-1670	203313	October 6, 1998
25	DNA76541-1675	203409	October 27, 1998
	DNA77301-1708	203407	October 27, 1998
	DNA77303-2502	203479	November 17, 1998
	DNA77648-1688	203408	October 27, 1998
	DNA77652-2505	203480	November 17, 1998
30	DNA83500-2506	203391	October 29, 1998
	DNA77568-1626	203134	August 18, 1998
	DNA23322-1393	203400	October 27, 1998
	DNA59814-1486	203359	October 20, 1998
	DNA62812-1594	203248	September 9, 1998
35	DNA66660-1585	203279	September 22, 1998
	DNA76393-1664	203323	October 6, 1998

These deposit were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC §122 and the Commissioner's rules pursuant thereto (including 37 CFR §1.14 with particular reference to 886 OG 638).

The assignee of the present application has agreed that if a culture of the materials on deposit should die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on notification with another of the same. Availability of the deposited material is not to be construed as a license

to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs
5 that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing
10 description and fall within the scope of the appended claims.

WHAT IS CLAIMED IS:

1. An isolated nucleic acid having at least 80% sequence identity to a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:4), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 8 (SEQ ID NO:10), Figure 10 (SEQ ID NO:12), Figure 12 (SEQ ID NO:17), Figure 14 (SEQ ID NO:22), Figure 16 (SEQ ID NO:24), Figure 18 (SEQ ID NO:29), Figure 20 (SEQ ID NO:31), Figure 22 (SEQ ID NO:33), Figure 24 (SEQ ID NO:41), Figure 26 (SEQ ID NO:43), Figure 28 (SEQ ID NO:50), Figure 30 (SEQ ID NO:52), Figure 32 (SEQ ID NO:54), Figure 34 (SEQ ID NO:56), Figure 36 (SEQ ID NO:58), Figure 38 (SEQ ID NO:63), Figure 40 (SEQ ID NO:68), Figure 42 (SEQ ID NO:70), Figure 44 (SEQ ID NO:72), Figure 46 (SEQ ID NO:77), Figure 48 (SEQ ID NO:79), Figure 50 (SEQ ID NO:84), Figure 52 (SEQ ID NO:86), Figure 54 (SEQ ID NO:88), Figure 56 (SEQ ID NO:95), Figure 58 (SEQ ID NO:100), Figure 60 (SEQ ID NO:102), Figure 62 (SEQ ID NO:104), Figure 64 (SEQ ID NO:111), Figure 66 (SEQ ID NO:116), Figure 68 (SEQ ID NO:118), Figure 70 (SEQ ID NO:123), Figure 72 (SEQ ID NO:128), Figure 74 (SEQ ID NO:130), Figure 76 (SEQ ID NO:132), Figure 78 (SEQ ID NO:134), Figure 80 (SEQ ID NO:136), Figure 82 (SEQ ID NO:138), Figure 84 (SEQ ID NO:140), Figure 86 (SEQ ID NO:142), Figure 88 (SEQ ID NO:144), Figure 90 (SEQ ID NO:146), Figure 92 (SEQ ID NO:148), Figure 94 (SEQ ID NO:153), Figure 96 (SEQ ID NO:158), Figure 98 (SEQ ID NO:160), Figure 100 (SEQ ID NO:162), Figure 102 (SEQ ID NO:170), Figure 104 (SEQ ID NO:180), Figure 106 (SEQ ID NO:189), Figure 108 (SEQ ID NO:194), Figure 110 (SEQ ID NO:196), Figure 112 (SEQ ID NO:198), Figure 114 (SEQ ID NO:203), Figure 116 (SEQ ID NO:210), Figure 118 (SEQ ID NO:212), Figure 120 (SEQ ID NO:214), Figure 122 (SEQ ID NO:216), Figure 124 (SEQ ID NO:218), Figure 126 (SEQ ID NO:220), Figure 128 (SEQ ID NO:225), Figure 130 (SEQ ID NO:227), Figure 132 (SEQ ID NO:229), Figure 134 (SEQ ID NO:234), Figure 136 (SEQ ID NO:236), Figure 138 (SEQ ID NO:243), Figure 140 (SEQ ID NO:248), Figure 142 (SEQ ID NO:253), Figure 144 (SEQ ID NO:260), Figure 146 (SEQ ID NO:265), Figure 148 (SEQ ID NO:267), Figure 150 (SEQ ID NO:269), Figure 152 (SEQ ID NO:271), Figure 154 (SEQ ID NO:273), Figure 156 (SEQ ID NO:275), Figure 158 (SEQ ID NO:277), Figure 160 (SEQ ID NO:282), Figure 162 (SEQ ID NO:287), Figure 164 (SEQ ID NO:292), Figure 166 (SEQ ID NO:297), Figure 168 (SEQ ID NO:302), Figure 170 (SEQ ID NO:304), Figure 172 (SEQ ID NO:306), Figure 174 (SEQ ID NO:308), Figure 176 (SEQ ID NO:310), Figure 178 (SEQ ID NO:315), Figure 180 (SEQ ID NO:317), Figure 182 (SEQ ID NO:322), Figure 184 (SEQ ID NO:324), Figure 186 (SEQ ID NO:326), Figure 188 (SEQ ID NO:328), Figure 190 (SEQ ID NO:330), Figure 192 (SEQ ID NO:332), Figure 194 (SEQ ID NO:334), Figure 196 (SEQ ID NO:336), Figure 198 (SEQ ID NO:338), Figure 200 (SEQ ID NO:340), Figure 202 (SEQ ID NO:347), Figure 204 (SEQ ID NO:352), Figure 206 (SEQ ID NO:354), Figure 208 (SEQ ID NO:356), Figure 210 (SEQ ID NO:358), Figure 212 (SEQ ID NO:364), Figure 214 (SEQ ID NO:366), Figure 216 (SEQ ID NO:372), Figure 218 (SEQ ID NO:374), Figure 220 (SEQ ID NO:376), Figure 222 (SEQ ID NO:378), Figure 224 (SEQ ID NO:383), Figure 226 (SEQ ID NO:385), Figure 228 (SEQ ID NO:390), Figure 230 (SEQ ID NO:395), Figure 232 (SEQ ID NO:397), Figure 234 (SEQ ID NO:402), Figure 236 (SEQ ID NO:406), Figure 238 (SEQ ID NO:410), Figure 240 (SEQ ID NO:415), Figure 242 (SEQ ID NO:423), Figure 244 (SEQ ID NO:429) and Figure 246 (SEQ ID NO:431).

2. The nucleic acid of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the sequence shown in Figure 1 (SEQ ID NO:3), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 7 (SEQ ID NO:9), Figure 9 (SEQ ID NO:11), Figure 11 (SEQ ID NO:16), Figure 13 (SEQ ID NO:21), Figure 15 (SEQ ID NO:23), Figure 17 (SEQ ID NO:28), Figure 19 (SEQ ID NO:30), Figure 21 (SEQ ID NO:32), Figure 23 (SEQ ID NO:40), Figure 25 (SEQ ID NO:42), Figure 27 (SEQ ID NO:49), Figure 29 (SEQ ID NO:51), Figure 31 (SEQ ID NO:53), Figure 33 (SEQ ID NO:55), Figure 35 (SEQ ID NO:57), Figure 37 (SEQ ID NO:62), Figure 39 (SEQ ID NO:67), Figure 41 (SEQ ID NO:69), Figure 43 (SEQ ID NO:71), Figure 45 (SEQ ID NO:76), Figure 47 (SEQ ID NO:78), Figure 49 (SEQ ID NO:83), Figure 51 (SEQ ID NO:85), Figure 53 (SEQ ID NO:87), Figure 55 (SEQ ID NO:94), Figure 57 (SEQ ID NO:99), Figure 59 (SEQ ID NO:101), Figure 61 (SEQ ID NO:103), Figure 63 (SEQ ID NO:110), Figure 65 (SEQ ID NO:115), Figure 67 (SEQ ID NO:117), Figure 69 (SEQ ID NO:122), Figure 71 (SEQ ID NO:127), Figure 73 (SEQ ID NO:129), Figure 75 (SEQ ID NO:131), Figure 77 (SEQ ID NO:133), Figure 79 (SEQ ID NO:135), Figure 81 (SEQ ID NO:137), Figure 83 (SEQ ID NO:139), Figure 85 (SEQ ID NO:141), Figure 87 (SEQ ID NO:143), Figure 89 (SEQ ID NO:145), Figure 91 (SEQ ID NO:147), Figure 93 (SEQ ID NO:152), Figure 95 (SEQ ID NO:157), Figure 97 (SEQ ID NO:159), Figure 99 (SEQ ID NO:161), Figure 101 (SEQ ID NO:169), Figure 103 (SEQ ID NO:179), Figure 105 (SEQ ID NO:188), Figure 107 (SEQ ID NO:193), Figure 109 (SEQ ID NO:195), Figure 111 (SEQ ID NO:197), Figure 113 (SEQ ID NO:202), Figure 115 (SEQ ID NO:209), Figure 117 (SEQ ID NO:211), Figure 119 (SEQ ID NO:213), Figure 121 (SEQ ID NO:215), Figure 123 (SEQ ID NO:217), Figure 125 (SEQ ID NO:219), Figure 127 (SEQ ID NO:224), Figure 129 (SEQ ID NO:226), Figure 131 (SEQ ID NO:228), Figure 133 (SEQ ID NO:233), Figure 135 (SEQ ID NO:235), Figure 137 (SEQ ID NO:242), Figure 139 (SEQ ID NO:247), Figure 141 (SEQ ID NO:252), Figure 143 (SEQ ID NO:259), Figure 145 (SEQ ID NO:264), Figure 147 (SEQ ID NO:266), Figure 149 (SEQ ID NO:268), Figure 151 (SEQ ID NO:270), Figure 153 (SEQ ID NO:272), Figure 155 (SEQ ID NO:274), Figure 157 (SEQ ID NO:276), Figure 159 (SEQ ID NO:281), Figure 161 (SEQ ID NO:286), Figure 163 (SEQ ID NO:291), Figure 165 (SEQ ID NO:296), Figure 167 (SEQ ID NO:301), Figure 169 (SEQ ID NO:303), Figure 171 (SEQ ID NO:305), Figure 173 (SEQ ID NO:307), Figure 175 (SEQ ID NO:309), Figure 177 (SEQ ID NO:314), Figure 179 (SEQ ID NO:316), Figure 181 (SEQ ID NO:321), Figure 183 (SEQ ID NO:323), Figure 185 (SEQ ID NO:325), Figure 187 (SEQ ID NO:327), Figure 189 (SEQ ID NO:329), Figure 191 (SEQ ID NO:331), Figure 193 (SEQ ID NO:333), Figure 195 (SEQ ID NO:335), Figure 197 (SEQ ID NO:337), Figure 199 (SEQ ID NO:339), Figure 201 (SEQ ID NO:346), Figure 203 (SEQ ID NO:351), Figure 205 (SEQ ID NO:353), Figure 207 (SEQ ID NO:355), Figure 209 (SEQ ID NO:357), Figure 211 (SEQ ID NO:363), Figure 213 (SEQ ID NO:365), Figure 215 (SEQ ID NO:371), Figure 217 (SEQ ID NO:373), Figure 219 (SEQ ID NO:375), Figure 221 (SEQ ID NO:377), Figure 223 (SEQ ID NO:382), Figure 225 (SEQ ID NO:384), Figure 227 (SEQ ID NO:389), Figure 229 (SEQ ID NO:394), Figure 231 (SEQ ID NO:396), Figure 233 (SEQ ID NO:401), Figure 235 (SEQ ID NO:405), Figure 237 (SEQ ID NO:409), Figure 239 (SEQ ID NO:414), Figure 241 (SEQ ID NO:422), Figure 242 (SEQ ID NO:428) and Figure 245 (SEQ ID NO:430).

3. The nucleic acid of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the full-length coding sequence of the sequence shown in Figure 1 (SEQ ID NO:3), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 7 (SEQ ID NO:9), Figure 9 (SEQ ID NO:11), Figure 11 (SEQ ID NO:16), Figure 13 (SEQ ID NO:21), Figure 15 (SEQ ID NO:23), Figure 17 (SEQ ID NO:28), Figure 19 (SEQ ID NO:30), Figure 21 (SEQ ID NO:32), Figure 23 (SEQ ID NO:40), Figure 25 (SEQ ID NO:42), Figure 27 (SEQ ID NO:49), Figure 29 (SEQ ID NO:51), Figure 31 (SEQ ID NO:53), Figure 33 (SEQ ID NO:55), Figure 35 (SEQ ID NO:57), Figure 37 (SEQ ID NO:62), Figure 39 (SEQ ID NO:67), Figure 41 (SEQ ID NO:69), Figure 43 (SEQ ID NO:71), Figure 45 (SEQ ID NO:76), Figure 47 (SEQ ID NO:78), Figure 49 (SEQ ID NO:83), Figure 51 (SEQ ID NO:85), Figure 53 (SEQ ID NO:87), Figure 55 (SEQ ID NO:94), Figure 57 (SEQ ID NO:99), Figure 59 (SEQ ID NO:101), Figure 61 (SEQ ID NO:103), Figure 63 (SEQ ID NO:110), Figure 65 (SEQ ID NO:115), Figure 67 (SEQ ID NO:117), Figure 69 (SEQ ID NO:122), Figure 71 (SEQ ID NO:127), Figure 73 (SEQ ID NO:129), Figure 75 (SEQ ID NO:131), Figure 77 (SEQ ID NO:133), Figure 79 (SEQ ID NO:135), Figure 81 (SEQ ID NO:137), Figure 83 (SEQ ID NO:139), Figure 85 (SEQ ID NO:141), Figure 87 (SEQ ID NO:143), Figure 89 (SEQ ID NO:145), Figure 91 (SEQ ID NO:147), Figure 93 (SEQ ID NO:152), Figure 95 (SEQ ID NO:157), Figure 97 (SEQ ID NO:159), Figure 99 (SEQ ID NO:161), Figure 101 (SEQ ID NO:169), Figure 103 (SEQ ID NO:179), Figure 105 (SEQ ID NO:188), Figure 107 (SEQ ID NO:193), Figure 109 (SEQ ID NO:195), Figure 111 (SEQ ID NO:197), Figure 113 (SEQ ID NO:202), Figure 115 (SEQ ID NO:209), Figure 117 (SEQ ID NO:211), Figure 119 (SEQ ID NO:213), Figure 121 (SEQ ID NO:215), Figure 123 (SEQ ID NO:217), Figure 125 (SEQ ID NO:219), Figure 127 (SEQ ID NO:224), Figure 129 (SEQ ID NO:226), Figure 131 (SEQ ID NO:228), Figure 133 (SEQ ID NO:233), Figure 135 (SEQ ID NO:235), Figure 137 (SEQ ID NO:242), Figure 139 (SEQ ID NO:247), Figure 141 (SEQ ID NO:252), Figure 143 (SEQ ID NO:259), Figure 145 (SEQ ID NO:264), Figure 147 (SEQ ID NO:266), Figure 149 (SEQ ID NO:268), Figure 151 (SEQ ID NO:270), Figure 153 (SEQ ID NO:272), Figure 155 (SEQ ID NO:274), Figure 157 (SEQ ID NO:276), Figure 159 (SEQ ID NO:281), Figure 161 (SEQ ID NO:286), Figure 163 (SEQ ID NO:291), Figure 165 (SEQ ID NO:296), Figure 167 (SEQ ID NO:301), Figure 169 (SEQ ID NO:303), Figure 171 (SEQ ID NO:305), Figure 173 (SEQ ID NO:307), Figure 175 (SEQ ID NO:309), Figure 177 (SEQ ID NO:314), Figure 179 (SEQ ID NO:316), Figure 181 (SEQ ID NO:321), Figure 183 (SEQ ID NO:323), Figure 185 (SEQ ID NO:325), Figure 187 (SEQ ID NO:327), Figure 189 (SEQ ID NO:329), Figure 191 (SEQ ID NO:331), Figure 193 (SEQ ID NO:333), Figure 195 (SEQ ID NO:335), Figure 197 (SEQ ID NO:337), Figure 199 (SEQ ID NO:339), Figure 201 (SEQ ID NO:346), Figure 203 (SEQ ID NO:351), Figure 205 (SEQ ID NO:353), Figure 207 (SEQ ID NO:355), Figure 209 (SEQ ID NO:357), Figure 211 (SEQ ID NO:363), Figure 213 (SEQ ID NO:365), Figure 215 (SEQ ID NO:371), Figure 217 (SEQ ID NO:373), Figure 219 (SEQ ID NO:375), Figure 221 (SEQ ID NO:377), Figure 223 (SEQ ID NO:382), Figure 225 (SEQ ID NO:384), Figure 227 (SEQ ID NO:389), Figure 229 (SEQ ID NO:394), Figure 231 (SEQ ID NO:396), Figure 233 (SEQ ID NO:401), Figure 235 (SEQ ID NO:405), Figure 237 (SEQ ID NO:409), Figure 239 (SEQ ID NO:414), Figure 241 (SEQ ID NO:422), Figure 242 (SEQ ID NO:428) and Figure 245 (SEQ ID NO:430).

4. Isolated nucleic acid which comprises the full-length coding sequence of the DNA deposited under any ATCC accession number shown in Table 2.
5. A vector comprising the nucleic acid of Claim 1.
- 5 6. The vector of Claim 5 operably linked to control sequences recognized by a host cell transformed with the vector.
7. A host cell comprising the vector of Claim 5.
- 10 8. The host cell of Claim 7 wherein said cell is a CHO cell.
9. The host cell of Claim 7 wherein said cell is an *E. coli*.
10. The host cell of Claim 7 wherein said cell is a yeast cell.
- 15 11. A process for producing a PRO polypeptides comprising culturing the host cell of Claim 7 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.
- 20 12. Isolated PRO polypeptide having at least 80% sequence identity to an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:4), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 8 (SEQ ID NO:10), Figure 10 (SEQ ID NO:12), Figure 12 (SEQ ID NO:17), Figure 14 (SEQ ID NO:22), Figure 16 (SEQ ID NO:24), Figure 18 (SEQ ID NO:29), Figure 20 (SEQ ID NO:31), Figure 22 (SEQ ID NO:33), Figure 24 (SEQ ID NO:41), Figure 26 (SEQ ID NO:43), Figure 28 (SEQ ID NO:50), Figure 30 (SEQ ID NO:52), Figure 32 (SEQ ID NO:54), Figure 34 (SEQ ID NO:56), Figure 36 (SEQ ID NO:58), Figure 38 (SEQ ID NO:63), Figure 40 (SEQ ID NO:68), Figure 42 (SEQ ID NO:70), Figure 44 (SEQ ID NO:72), Figure 46 (SEQ ID NO:77), Figure 48 (SEQ ID NO:79), Figure 50 (SEQ ID NO:84), Figure 52 (SEQ ID NO:86), Figure 54 (SEQ ID NO:88), Figure 56 (SEQ ID NO:95), Figure 58 (SEQ ID NO:100), Figure 60 (SEQ ID NO:102), Figure 62 (SEQ ID NO:104), Figure 64 (SEQ ID NO:111), Figure 66 (SEQ ID NO:116), Figure 68 (SEQ ID NO:118), Figure 70 (SEQ ID NO:123), Figure 72 (SEQ ID NO:128), Figure 74 (SEQ ID NO:130), Figure 76 (SEQ ID NO:132), Figure 78 (SEQ ID NO:134), Figure 80 (SEQ ID NO:136), Figure 82 (SEQ ID NO:138), Figure 84 (SEQ ID NO:140), Figure 86 (SEQ ID NO:142), Figure 88 (SEQ ID NO:144), Figure 90 (SEQ ID NO:146), Figure 92 (SEQ ID NO:148), Figure 94 (SEQ ID NO:153), Figure 96 (SEQ ID NO:158), Figure 98 (SEQ ID NO:160), Figure 100 (SEQ ID NO:162), Figure 102 (SEQ ID NO:170), Figure 104 (SEQ ID NO:180), Figure 106 (SEQ ID NO:189), Figure 108 (SEQ ID NO:194), Figure 110 (SEQ ID NO:196), Figure 112 (SEQ ID NO:198), Figure 114 (SEQ ID NO:203), Figure 116 (SEQ ID NO:210), Figure 118 (SEQ ID NO:212), Figure 120 (SEQ ID NO:214), Figure 122 (SEQ ID NO:216).

NO:216), Figure 124 (SEQ ID NO:218), Figure 126 (SEQ ID NO:220), Figure 128 (SEQ ID NO:225), Figure 130 (SEQ ID NO:227), Figure 132 (SEQ ID NO:229), Figure 134 (SEQ ID NO:234), Figure 136 (SEQ ID NO:236), Figure 138 (SEQ ID NO:243), Figure 140 (SEQ ID NO:248), Figure 142 (SEQ ID NO:253), Figure 144 (SEQ ID NO:260), Figure 146 (SEQ ID NO:265), Figure 148 (SEQ ID NO:267), Figure 150 (SEQ ID NO:269), Figure 152 (SEQ ID NO:271), Figure 154 (SEQ ID NO:273), Figure 156 (SEQ ID NO:275), Figure 158 (SEQ ID NO:277), Figure 160 (SEQ ID NO:282), Figure 162 (SEQ ID NO:287), Figure 164 (SEQ ID NO:292), Figure 166 (SEQ ID NO:297), Figure 168 (SEQ ID NO:302), Figure 170 (SEQ ID NO:304), Figure 172 (SEQ ID NO:306), Figure 174 (SEQ ID NO:308), Figure 176 (SEQ ID NO:310), Figure 178 (SEQ ID NO:315), Figure 180 (SEQ ID NO:317), Figure 182 (SEQ ID NO:322), Figure 184 (SEQ ID NO:324), Figure 186 (SEQ ID NO:326), Figure 188 (SEQ ID NO:328), Figure 190 (SEQ ID NO:330), Figure 192 (SEQ ID NO:332), Figure 194 (SEQ ID NO:334), Figure 196 (SEQ ID NO:336), Figure 198 (SEQ ID NO:338), Figure 200 (SEQ ID NO:340), Figure 202 (SEQ ID NO:347), Figure 204 (SEQ ID NO:352), Figure 206 (SEQ ID NO:354), Figure 208 (SEQ ID NO:356), Figure 210 (SEQ ID NO:358), Figure 212 (SEQ ID NO:364), Figure 214 (SEQ ID NO:366), Figure 216 (SEQ ID NO:372), Figure 218 (SEQ ID NO:374), Figure 220 (SEQ ID NO:376), Figure 222 (SEQ ID NO:378), Figure 224 (SEQ ID NO:383), Figure 226 (SEQ ID NO:385), Figure 228 (SEQ ID NO:390), Figure 230 (SEQ ID NO:395), Figure 232 (SEQ ID NO:397), Figure 234 (SEQ ID NO:402), Figure 236 (SEQ ID NO:406), Figure 238 (SEQ ID NO:410), Figure 240 (SEQ ID NO:415), Figure 242 (SEQ ID NO:423), Figure 244 (SEQ ID NO:429) and Figure 246 (SEQ ID NO:431).

13. Isolated PRO polypeptide having at least 80% sequence identity to the amino acid sequence encoded by a nucleic acid molecule deposited under any ATCC accession number shown in Table 2.

14. A chimeric molecule comprising a polypeptide according to Claim 12 fused to a heterologous amino acid sequence.

15. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is an epitope tag sequence.

16. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is a Fc region of an immunoglobulin.

17. An antibody which specifically binds to a PRO polypeptide according to Claim 12.

18. The antibody of Claim 17 wherein said antibody is a monoclonal antibody.

19. The antibody of Claim 17 wherein said antibody is a humanized antibody.

20. The antibody of Claim 17 wherein said antibody is an antibody fragment.

21. An isolated nucleic acid which has at least 80% sequence identity to a nucleic acid sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:3), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 7 (SEQ ID NO:9), Figure 9 (SEQ ID NO:11), Figure 11 (SEQ ID NO:16), Figure 13 (SEQ ID NO:21), Figure 15 (SEQ ID NO:23), Figure 17 (SEQ ID NO:28), Figure 19 (SEQ ID NO:30), Figure 21 (SEQ ID NO:32), Figure 23 (SEQ ID NO:40), Figure 25 (SEQ ID NO:42), Figure 27 (SEQ ID NO:49), Figure 29 (SEQ ID NO:51), Figure 31 (SEQ ID NO:53), Figure 33 (SEQ ID NO:55), Figure 35 (SEQ ID NO:57), Figure 37 (SEQ ID NO:62), Figure 39 (SEQ ID NO:67), Figure 41 (SEQ ID NO:69), Figure 43 (SEQ ID NO:71), Figure 45 (SEQ ID NO:76), Figure 47 (SEQ ID NO:78), Figure 49 (SEQ ID NO:83), Figure 51 (SEQ ID NO:85), Figure 53 (SEQ ID NO:87), Figure 55 (SEQ ID NO:94), Figure 57 (SEQ ID NO:99), Figure 59 (SEQ ID NO:101), Figure 61 (SEQ ID NO:103), Figure 63 (SEQ ID NO:110), Figure 65 (SEQ ID NO:115), Figure 67 (SEQ ID NO:117), Figure 69 (SEQ ID NO:122), Figure 71 (SEQ ID NO:127), Figure 73 (SEQ ID NO:129), Figure 75 (SEQ ID NO:131), Figure 77 (SEQ ID NO:133), Figure 79 (SEQ ID NO:135), Figure 81 (SEQ ID NO:137), Figure 83 (SEQ ID NO:139), Figure 85 (SEQ ID NO:141), Figure 87 (SEQ ID NO:143), Figure 89 (SEQ ID NO:145), Figure 91 (SEQ ID NO:147), Figure 93 (SEQ ID NO:152), Figure 95 (SEQ ID NO:157), Figure 97 (SEQ ID NO:159), Figure 99 (SEQ ID NO:161), Figure 101 (SEQ ID NO:169), Figure 103 (SEQ ID NO:179), Figure 105 (SEQ ID NO:188), Figure 107 (SEQ ID NO:193), Figure 109 (SEQ ID NO:195), Figure 111 (SEQ ID NO:197), Figure 113 (SEQ ID NO:202), Figure 115 (SEQ ID NO:209), Figure 117 (SEQ ID NO:211), Figure 119 (SEQ ID NO:213), Figure 121 (SEQ ID NO:215), Figure 123 (SEQ ID NO:217), Figure 125 (SEQ ID NO:219), Figure 127 (SEQ ID NO:224), Figure 129 (SEQ ID NO:226), Figure 131 (SEQ ID NO:228), Figure 133 (SEQ ID NO:233), Figure 135 (SEQ ID NO:235), Figure 137 (SEQ ID NO:242), Figure 139 (SEQ ID NO:247), Figure 141 (SEQ ID NO:252), Figure 143 (SEQ ID NO:259), Figure 145 (SEQ ID NO:264), Figure 147 (SEQ ID NO:266), Figure 149 (SEQ ID NO:268), Figure 151 (SEQ ID NO:270), Figure 153 (SEQ ID NO:272), Figure 155 (SEQ ID NO:274), Figure 157 (SEQ ID NO:276), Figure 159 (SEQ ID NO:281), Figure 161 (SEQ ID NO:286), Figure 163 (SEQ ID NO:291), Figure 165 (SEQ ID NO:296), Figure 167 (SEQ ID NO:301), Figure 169 (SEQ ID NO:303), Figure 171 (SEQ ID NO:305), Figure 173 (SEQ ID NO:307), Figure 175 (SEQ ID NO:309), Figure 177 (SEQ ID NO:314), Figure 179 (SEQ ID NO:316), Figure 181 (SEQ ID NO:321), Figure 183 (SEQ ID NO:323), Figure 185 (SEQ ID NO:325), Figure 187 (SEQ ID NO:327), Figure 189 (SEQ ID NO:329), Figure 191 (SEQ ID NO:331), Figure 193 (SEQ ID NO:333), Figure 195 (SEQ ID NO:335), Figure 197 (SEQ ID NO:337), Figure 199 (SEQ ID NO:339), Figure 201 (SEQ ID NO:346), Figure 203 (SEQ ID NO:351), Figure 205 (SEQ ID NO:353), Figure 207 (SEQ ID NO:355), Figure 209 (SEQ ID NO:357), Figure 211 (SEQ ID NO:363), Figure 213 (SEQ ID NO:365), Figure 215 (SEQ ID NO:371), Figure 217 (SEQ ID NO:373), Figure 219 (SEQ ID NO:375), Figure 221 (SEQ ID NO:377), Figure 223 (SEQ ID NO:382), Figure 225 (SEQ ID NO:384), Figure 227 (SEQ ID NO:389), Figure 229 (SEQ ID NO:394), Figure 231 (SEQ ID NO:396), Figure 233 (SEQ ID NO:401), Figure 235 (SEQ ID NO:405), Figure 237 (SEQ ID NO:409), Figure 239 (SEQ ID NO:414), Figure 241 (SEQ ID NO:422), Figure 242 (SEQ ID NO:428) and Figure 245 (SEQ ID NO:430).

22. An isolated nucleic acid which has at least 80% sequence identity to the full-length coding sequence of a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:3), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 7 (SEQ ID NO:9), Figure 9 (SEQ ID NO:11), Figure 11 (SEQ ID NO:16), Figure 13 (SEQ ID NO:21), Figure 15 (SEQ ID NO:23), Figure 17 (SEQ ID NO:28), Figure 19 (SEQ ID NO:30), Figure 21 (SEQ ID NO:32), Figure 23 (SEQ ID NO:40), Figure 25 (SEQ ID NO:42), Figure 27 (SEQ ID NO:49), Figure 29 (SEQ ID NO:51), Figure 31 (SEQ ID NO:53), Figure 33 (SEQ ID NO:55), Figure 35 (SEQ ID NO:57), Figure 37 (SEQ ID NO:62), Figure 39 (SEQ ID NO:67), Figure 41 (SEQ ID NO:69), Figure 43 (SEQ ID NO:71), Figure 45 (SEQ ID NO:76), Figure 47 (SEQ ID NO:78), Figure 49 (SEQ ID NO:83), Figure 51 (SEQ ID NO:85), Figure 53 (SEQ ID NO:87), Figure 55 (SEQ ID NO:94), Figure 57 (SEQ ID NO:99), Figure 59 (SEQ ID NO:101), Figure 61 (SEQ ID NO:103), Figure 63 (SEQ ID NO:110), Figure 65 (SEQ ID NO:115), Figure 67 (SEQ ID NO:117), Figure 69 (SEQ ID NO:122), Figure 71 (SEQ ID NO:127), Figure 73 (SEQ ID NO:129), Figure 75 (SEQ ID NO:131), Figure 77 (SEQ ID NO:133), Figure 79 (SEQ ID NO:135), Figure 81 (SEQ ID NO:137), Figure 83 (SEQ ID NO:139), Figure 85 (SEQ ID NO:141), Figure 87 (SEQ ID NO:143), Figure 89 (SEQ ID NO:145), Figure 91 (SEQ ID NO:147), Figure 93 (SEQ ID NO:152), Figure 95 (SEQ ID NO:157), Figure 97 (SEQ ID NO:159), Figure 99 (SEQ ID NO:161), Figure 101 (SEQ ID NO:169), Figure 103 (SEQ ID NO:179), Figure 105 (SEQ ID NO:188), Figure 107 (SEQ ID NO:193), Figure 109 (SEQ ID NO:195), Figure 111 (SEQ ID NO:197), Figure 113 (SEQ ID NO:202), Figure 115 (SEQ ID NO:209), Figure 117 (SEQ ID NO:211), Figure 119 (SEQ ID NO:213), Figure 121 (SEQ ID NO:215), Figure 123 (SEQ ID NO:217), Figure 125 (SEQ ID NO:219), Figure 127 (SEQ ID NO:224), Figure 129 (SEQ ID NO:226), Figure 131 (SEQ ID NO:228), Figure 133 (SEQ ID NO:233), Figure 135 (SEQ ID NO:235), Figure 137 (SEQ ID NO:242), Figure 139 (SEQ ID NO:247), Figure 141 (SEQ ID NO:252), Figure 143 (SEQ ID NO:259), Figure 145 (SEQ ID NO:264), Figure 147 (SEQ ID NO:266), Figure 149 (SEQ ID NO:268), Figure 151 (SEQ ID NO:270), Figure 153 (SEQ ID NO:272), Figure 155 (SEQ ID NO:274), Figure 157 (SEQ ID NO:276), Figure 159 (SEQ ID NO:281), Figure 161 (SEQ ID NO:286), Figure 163 (SEQ ID NO:291), Figure 165 (SEQ ID NO:296), Figure 167 (SEQ ID NO:301), Figure 169 (SEQ ID NO:303), Figure 171 (SEQ ID NO:305), Figure 173 (SEQ ID NO:307), Figure 175 (SEQ ID NO:309), Figure 177 (SEQ ID NO:314), Figure 179 (SEQ ID NO:316), Figure 181 (SEQ ID NO:321), Figure 183 (SEQ ID NO:323), Figure 185 (SEQ ID NO:325), Figure 187 (SEQ ID NO:327), Figure 189 (SEQ ID NO:329), Figure 191 (SEQ ID NO:331), Figure 193 (SEQ ID NO:333), Figure 195 (SEQ ID NO:335), Figure 197 (SEQ ID NO:337), Figure 199 (SEQ ID NO:339), Figure 201 (SEQ ID NO:346), Figure 203 (SEQ ID NO:351), Figure 205 (SEQ ID NO:353), Figure 207 (SEQ ID NO:355), Figure 209 (SEQ ID NO:357), Figure 211 (SEQ ID NO:363), Figure 213 (SEQ ID NO:365), Figure 215 (SEQ ID NO:371), Figure 217 (SEQ ID NO:373), Figure 219 (SEQ ID NO:375), Figure 221 (SEQ ID NO:377), Figure 223 (SEQ ID NO:382), Figure 225 (SEQ ID NO:384), Figure 227 (SEQ ID NO:389), Figure 229 (SEQ ID NO:394), Figure 231 (SEQ ID NO:396), Figure 233 (SEQ ID NO:401), Figure 235 (SEQ ID NO:405), Figure 237 (SEQ ID NO:409), Figure 239 (SEQ ID NO:414), Figure 241 (SEQ ID NO:422), Figure 242 (SEQ ID NO:428) and Figure 245 (SEQ ID NO:430).

23. An isolated extracellular domain of a PRO polypeptide.

24. An isolated PRO polypeptide lacking its associated signal peptide.
25. An isolated polypeptide having at least about 80% amino acid sequence identity to an extracellular domain of of PRO polypeptide.
- 5 26. An isolated polypeptide having at least about 80% amino acid sequence identity to a PRO polypeptide lacking its associated signal peptide.
27. An isolated nucleic acid encoding the polypeptide of any one of Claims 23 to 26.

FIGURE 1

CCAATCGCCCGGTGCGGTGGTGCAGGGTCTCGGGCTAGTCATGGCGTCCCCGTCTCGGAGAC
TGCAGACTAAACCAGTCATTACTTGTTTCAAGAGCGTTCTGCTAATCTACACTTTTATTTTC
TGGATCACTGGCGTTATCCTTCTTGCACTTGGCATTGTTGGGGCAAGGTGAGCCTGGAGAATTA
CTTTTCTCTTTTAAATGAGAAGGCCACCAATGTCCCCTTCGTGCTCATTGCTACTGGTACCG
TCATTATTCTTTTGGGCACCTTTGGTTGTTTTGCTACCTGCCGAGCTTCTGCATGGATGCTA
AAACTGTATGCAATGTTTCTGACTCTCGTTTTTTTTGGTTCGAACTGGTCGCTGCCATCGTAGG
ATTTGTTTTTCAGACATGAGATTAAGAACAGCTTTAAGAATAATTATGAGAAGGCTTTGAAGC
AGTATAACTCTACAGGAGATTATAGAAGCCATGCAGTAGACAAGATCCAAAATACGTTGCAT
TGTTGTGGTGTCAACGATTATAGAGATTGGACAGATACTAATTATTACTCAGAAAAAGGATT
TCCTAAGAGTTGCTGTAAACTTGAAGATTGTACTCCACAGAGAGATGCAGACAAAGTAAACA
ATGAAGGTTGTTTTATAAAGGTGATGACCATTATAGAGTCAGAAATGGGAGTCGTTGCAGGA
ATTCCTTTGGAGTTGCTTGCTTCCAACCTGATTGGAATCTTTCTCGCCTACTGCCWCTCTCG
TGCCATAACAAATAACCAGTATGAGATAGTGTAACCCAATGTATCTGTGGGCCTATTCCTCT
CTACCTTTAAGGACATTTAGGGTCCCCCCTGTGAATTAGAAAGTTGCTTGGCTGGAGAACTG
ACAACACTACTTACTGATAGACCAAAAACTACACCAGTAGGTTGATTCAATCAAGATGTAT
GTAGACCTAAACTACACCAATAGGCTGATTCAATCAAGATCCGTGCTCGCAGTGGGCTGAT
TCAATCAAGATGTATGTTTGCTATGTTCTAAGTCCACCTTCTATCCCATTTCATGTTAGATCG
TTGAAACCCTGTATCCCTCTGAAACACTGGAAGAGCTAGTAAATTGTAAATGAAGT

FIGURE 2

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA19902

><subunit 1 of 1, 245 aa, 1 stop, 1 unknown

><MW: -1, pI: 8.36, NX(S/T): 1

MASPSRRLQTKPVITCFKSVLLIYTFIFWITGVILLAVGIWGKVSLENYFSLLEKATNVPF
VLIATGTVIILLGTFGCFATCRASAWMLKLYAMFLTLVFLVELVAAIVGFVFRHEIKNSFKN
NYEKALKQYNSTGDYRSHAVDKIQNTLHCCGVTDYRDWTDTNYYSEKGFPSCKLEDCTPQ
RDADKVNNEGCFIKVMTIIESEMGVVAGISFGVACFQLIGIFLAYCXSRITNNQYEIV

Important features of the protein:

Signal peptide:

amino acids 1-42

Transmembrane domains:

amino acids 19-42, 61-83, 92-114, 209-230,

N-glycosylation site.

amino acids 134-138

Tyrosine kinase phosphorylation site.

amino acids 160-168, 160-169

N-myristoylation site.

amino acids 75-81, 78-84, 210-216, 214-220, 226-232

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 69-80, 211-222

FIGURE 3

CCCACGCGTCCGGCGCCGTGGCCTCGCGTCCATCTTTGCCGTTCTCTCGGACCTGTCAAAA
GGAGTCGCGCCGCGCCGCGCCGCCCCCTCCCTCCGGTGGGCCCCGGGAGGTAGAGAAAGTCAGT
GCCACAGCCCGACCGCGCTGCTCTGAGCCCTGGGCACGCGGAACGGGAGGGAGTCTGAGGGT
TGGGGACGTCTGTGAGGGAGGGGAACAGCCGCTCGAGCCTGGGGCGGGCGGACCGGACTGGG
GCCGGGGTAGGCTCTGGAAAGGGCCCCGGGAGAGAGGTGGCGTTGGTCAGAACCTGAGAAACA
GCCGAGAGGTTTTCCACCGAGGCCCGCGCTTGAGGGATCTGAAGAGGTTCTTAGAAGAGGGT
GTTCCCTCTTTCGGGGGTCTCACCAGAAGAGGTTCTTGGGGGTGCCCCCTTCTGAGGAGGCT
GCGGCTAACAGGGCCCAGAACTGCCATTGGATGTCCAGAATCCCCTGTAGTTGATAATGTTG
GGAATAAGCTCTGCAACTTTCTTTGGCATTTCAGTTGTTAAAAACAAATAGGATGCAAATTCC
TCAACTCCAGGTTATGAAAAACAGTACTTGGAAAACTGAAAACTACCTAAATGATCGTCTTTG
GTTGGGCCGTGTTCTTAGCGAGCAGAAGCCTTGGCCAGGGTCTGTTGTTGACTCTCGAAGAG
CACATAGCCCACTTCCTAGGGACTGGAGGTGCCGCTACTACCATGGGTAATTCCTGTATCTG
CCGAGATGACAGTGGAACAGATGACAGTGTTGACACCCAACAGCAACAGGCCGAGAACAGTG
CAGTACCCACTGCTGACACAAGGAGCCAACCACGGGACCCTGTTGCGGCCACCAAGGAGGGGC
CGAGGACCTCATGAGCCAAGGAGAAAGAAACAAAATGTGGATGGGCTAGTGTTGGACACACT
GGCAGTAATACGGACTCTTGTAGATAAGTAAAGTATCTGACTCACGGTCACCTCCAGTGGAAT
GAAAAGTGTTCTGCCCCGAACCATGACTTTAGGACTCCTTCAGTTCCTTTAGGACATACTCG
CCAAGCCTTGTGCTCACAGGGCAAAGGAGAATATTTTAATGCTCCGCTGATGGCAGAGTAAA
TGATAAGATTTGATGTTTTTGCTTGCTGTCATCTACTTTGTCTGGAAATGTCTAAATGTTTC
TGTAGCAGAAAACACGATAAAGCTATGATCTTTATTAGAG

FIGURE 4

MIVFGWAVFLASRSLGQGLLLTLEEHIAHFLGTGGAATTMGNSCICRDDSGTDDSVDTQQQQ
AENSAVPTADTRSQPRDPVRPPRRGRGPHEPRRKKQNV DGLVLDLAVIRTLVDKO

Signal peptide:

amino acids 1-16

Casein kinase II phosphorylation site.

amino acids 22-26, 50-54, 113-117

N-myristoylation site.

amino acids 18-24, 32-38, 34-40, 35-41, 51-57

FIGURE 5

GGCACGAGGCGCTGTCCACCCGGGGGCGTGGGAGTGAGGTACCAGATTAGCCCATTTGGCC
CCGACGCCTCTGTTCTCGGAATCCGGGTGCTGCGGATTGAGGTCCCGGTTCCCTAACGGACTG
CAAGATGGAGGAAGGCGGGAACCTAGGAGGCCTGATTAAAGATGGTCCATCTACTGGTCTTGT
CAGGTGCCTGGGGCATGCAAATGTGGGTGACCTTCGTCTCAGGCTTCCTGCTTTTCCGAAGC
CTTCCCCGACATACCTTCGGACTAGTGCAGAGCAAACCTCTTCCCCTTCTACTTCCACATCTC
CATGGGCTGTGCCTTCATCAACCTCTGCATCTTGGCTTCACAGCATGCTTGGGCTCAGCTCA
CATTCTGGGAGGCCAGCCAGCTTTACCTGCTGTTCTGAGCCTTACGCTGGCCACTGTCAAC
GCCCCGCTGGCTGGAACCCCGCACCACAGCTGCCATGTGGGCCCTGCAAACCGTGGAGAAGGA
GCGAGGCCTGGGTGGGGAGGTACCAGGCAGCCACCAGGGTCCCGATCCCTACCGCCAGCTGC
GAGAGAAGGACCCCAAGTACAGTGCTCTCCGCCAGAATTTCTTCCGCTACCATGGGCTGTCC
TCTCTTTGCAATCTGGGCTGCGTCCTGAGCAATGGGCTCTGTCTCGCTGGCCTTGCCCTGGA
AATAAGGAGCCTCTAGCATGGGCCCTGCATGCTAATAAATGCTTCTTCAGAAATGAAAAAA
AAAAAAAAAAAA

FIGURE 6

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56107

<subunit 1 of 1, 231 aa, 1 stop

<NX(S/T): 0

MEEGGNLGGLIKMVHLLVLSGAWGMQMWVTFVSGFLLFRSLPRHTFGLVQSKLFPFYFHISM

GCAFINLCILASQHAWAQLTFWEASQLYLLFLSLTLATVNARWLEPRTTAAMWALQTVEKER

GLGGEVPGSHQGPDPYRQLREKDPKYSALRQNFYHGLSSLCNLGCVLSNGLCLAGLALEIRSL

Signal peptide:

amino acids 1-24

Transmembrane domain:

amino acids 86-103, 60-75

Casein kinase II phosphorylation site.

amino acids 82-86

Tyrosine kinase phosphorylation site.

amino acids 144-151

N-myristoylation site.

amino acids 4-10, 5-11, 47-53, 170-176, 176-182

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 54-65

G-protein coupled receptors proteins.

amino acids 44-85

FIGURE 7

AATTCAGATTTTAAGCCCATCTGCAGTGGAATTCATGAACTAGCAAGAGGACACCATCTT
CTTGTATTATACAAGAAAGGAGTGTACCTATCACACACAGGGGGGAAAAATGCTCTTTTGGGT
GCTAGGCCTCCTAATCCTCTGTGGTTTTCTGTGGACTCGTAAAGGAAAATAAGATTGAAG
ACATCACTGATAAGTACATTTTTATCACTGGATGTGACTCGGGCTTTGGAACTTGGCAGCC
AGAACTTTTGATAAAAAGGGATTTTCATGTAATCGCTGCCTGTCTGACTGAATCAGGATCAAC
AGCTTTAAAGGCAGAAACCTCAGAGAGACTTCGTACTGTGCTTCTGGATGTGACCGACCCAG
AGAATGTCAAGAGGACTGCCCAGTGGGTGAAGAACCAAGTTGGGGAGAAAGGTCTCTGGGGT
CTGATCAATAATGCTGGTGTTCCTGGCGTGCTGGCTCCCCTGACTGGCTGACACTAGAGGA
CTACAGAGAACCTATTGAAGTGAACCTGTTTGGACTCATCAGTGTGACACTAAATATGCTTC
CTTTGGTCAAGAAAGCTCAAGGGAGAGTTATTAATGTCTCCAGTGTGGAGGTCGCCTTGCA
ATCGTTGGAGGGGGCTATACTCCATCCAAATATGCAGTGGAAGGTTTCAATGACAGCTTAAG
ACGGGACATGAAAGCTTTTGGTGTGCACGTCTCATGCATTGAACCAGGATTGTTCAAAACAA
ACTTGGCAGATCCAGTAAAGGTAATTGAAAAAACTCGCCATTTGGGAGCAGCTGTCTCCA
GACATCAAACAACAATATGGAGAAGGTTACATTGAAAAAAGTCTAGACAACTGAAAGGCAA
TAAATCCTATGTGAACATGGACCTCTCTCCGGTGGTAGAGTGCATGGACCACGCTCTAACAA
GTCTCTTCCCTAAGACTCATTATGCCGCTGGAAAAGATGCCAAAATTTTCTGGATACCTCTG
TCTCACATGCCAGCAGCTTTGCAAGACTTTTTATTGTTGAAACAGAAAGCAGAGCTGGCTAA
TCCCAAGGCAGTGTGACTCAGCTAACCACAAATGTCTCCTCCAGGCTATGAAATTGGCCGAT
TTCAAGAACACATCTCCTTTTCAACCCCATTCCTTATCTGCTCCAACCTGGACTCATTTAGA
TCGTGCTTATTTGGATTGCAAAGGGAGTCCCACCATCGCTGGTGGTATCCCAGGGTCCCTG
CTCAAGTTTTCTTTGAAAAGGAGGGCTGGAATGGTACATCACATAGGCAAGTCCTGCCCTGT
ATTTAGGCTTTGCCTGCTTGGTGTGATGTAAGGGAAATTGAAAGACTTGCCCATTCAAAATG
ATCTTTACCGTGGCCTGCCCCATGCTTATGGTCCCAGCATTTACAGTAACTTGTGAATGTT
AAGTATCATCTCTTATCTAAATATTAAGATAAGTCAACCCAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAA

FIGURE 8

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56406

><subunit 1 of 1, 319 aa, 1 stop

><MW: 35227, pI: 8.97, NX(S/T): 3

MLFWVLGLLILCGFLWTRKGKLIKIEDITDKYIFITGCDSGFGNLAARTFDKKGFHVIAACLT
ESGSTALKAETSERLRTVLLDVTDPENVKRTAQWVKNOVGEKGLWGLINNAGVPGVLAPTDW
LTLEDYREPIEVNLFGLISVTNLMLPLVKKAQGRVINVSSVGGRLAIVGGGYTPSKYAVEGF
NDSLRRDMKAFGVHVSCIEPGLFKTNLADPVKVIEKKLAIWEQLSPDIKQQYGEgyIEKSLD
KLKGNKSYVNMDLSPVVECMDHALTSLFPKTHYAAGKDAKIFWIPLSHMPAALQDFLLLKQK
AELANPKAV

Important features of the protein:

Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 136-152

N-glycosylation sites.

amino acids 161-163, 187-190 and 253-256

Glycosaminoglycan attachment site.

amino acids 39-42

N-myristoylation sites.

amino acids 36-41, 42-47, 108-113, 166-171, 198-203 and 207-212

FIGURE 9

GCGGGCTGTTGACGGCGCTGCGATGGCTGCCTGCGAGGGCAGGAGAAGCGGAGCTCTCGGTT
CCTCTCAGTCGGACTTCCTGACGCCGCCAGTGGGCGGGGCCCTTGGGCCGTCGCCACCACT
GTAGTCATGTACCCACCGCCGCCGCCGCCCTCATCGGGACTTCATCTCGGTGACGCTGAG
CTTTGGCGAGAGCTATGACAACAGCAAGAGTTGGCGGCGGCGCTCGTGCTGGAGGAAATGGA
AGCAACTGTGAGATTGCAGCGGAATATGATTCTCTTCTCCTTGCCTTTCTGCTTTTCTGT
GGACTCCTCTTCTACATCAACTTGGCTGACCATTGGAAAGCTCTGGCTTTCAGGCTAGAGGA
AGAGCAGAAGATGAGGCCAGAAATTGCTGGGTAAAACCAGCAAATCCACCCGTCTTACCAG
CTCCTCAGAAGGCGGACACCGACCCTGAGAACTTACCTGAGATTTCGTACAGAAGACACAA
AGACACATCCAGCGGGGACCACCTCACCTGCAGATTAGACCCCCAAGCCAAGACCTGAAGGA
TGGGACCCAGGAGGAGGCCACAAAAGGCAAGAAGCCCCTGTGGATCCCCGCCCGGAAGGAG
ATCCGCAGAGGACAGTCATCAGCTGGAGGGGAGCGGTGATCGAGCCTGAGCAGGGCACCGAG
CTCCCTTCAAGAAGAGCAGAAGTGCCACCAAGCCTCCCCTGCCACCGGCCAGGACACAGGG
CACACCAGTGCATCTGAACTATCGCCAGAAGGGCGTGATTGACGTCTTCTGTCATGCATGGA
AAGGATACCGCAAGTTTGTCATGGGGCCATGACGAGCTGAAGCCTGTGTCCAGGTCTTTCAGT
GAGTGGTTTGGCCTCGGTCTCACACTGATCGACGCGCTGGACACCATGTGGATCTTGGGTCT
GAGGAAAGAATTTGAGGAAGCCAGGAAGTGGGTGTGGAAGAAGTTACACTTTGAAAAGGACG
TGGACGTCAACCTGTTTGAGAGCACGATCCGCATCCTGGGGGGGCTCCTGAGTGCCTACCAC
CTGTCTGGGGACAGCCTCTTCTGAGGAAAGCTGAGGATTTTGGAAATCGGCTAATGCCTGC
CTTCAGAACACCATCCAAGATTCTTACTCGGATGTGAACATCGGTACTGGAGTTGCCACC
CGCCACGGTGGACCTCCGACAGCACTGTGGCCGAGGTGACCAGCATTGAGCTGGAGTTCCGG
GAGCTCTCCCGTCTCACAGGGGATAAGAAGTTTCAGGAGGCAGTGGAGAAGGTGACACAGCA
CATCCACGGCCTGTCTGGGAAGAAGGATGGGCTGGTGCCCATGTTTCATCAATACCCACAGTG
GCCTCTTACCCACCTGGGCGTATTCACGCTGGGCGCCAGGGCCGACAGCTACTATGAGTAC
CTGCTGAAGCAGTGGATCCAGGGCGGGAAGCAGGAGACACAGCTGCTGGAAGACTACGTGGA
AGCCATCGAGGGTGTGAGAACGCACCTGCTGCGGCACTCCGAGCCCAGTAAGCTCACCTTTG
TGGGGGAGCTTGCCACGGCCGCTTCAGTGCCAAGATGGACCACCTGGTGTGCTTCTGCCA
GGGACGCTGGCTCTGGGCGTCTACCACGGCCTGCCCGCCAGCCACATGGAGCTGGCCAGGA
GCTCATGGAGACTTGTTACCAGATGAACCGGCAGATGGAGACGGGGCTGAGTCCCGAGATCG
TGCACTTCAACCTTTACCCCCAGCCGGGCCGTCGGGACGTGGAGGTCAAGCCAGCAGACAGG
CACAACCTGCTGCGGCCAGAGACCGTGGAGAGCCTGTTCTACCTGTACCGCGTCACAGGGGA
CCGCAAATACCAGGACTGGGGCTGGGAGATTCTGCAGAGCTTCAGCCGATTACACGGGTCC
CCTCGGGTGGCTATTCTTCCATCAACAATGTCCAGGATCCTCAGAAGCCCGAGCCTAGGGAC
AAGATGGAGAGCTTCTTCTGGGGGAGACGCTCAAGTATCTGTTCTTGCTCTTCTCCGATGA
CCCAAACCTGCTCAGCCTGGACGCCTACGTGTTCAACACCGAAGCCCACCTCTGCCTATCT
GGACCCCTGCCTAGGGTGGATGGCTGCTGGTGTGGGGACTTCGGGTGGGCAGAGGCACCTTG
CTGGGTCTGTGGCATTTCCTCAAGGGCCACGTAGCACCGGCAACCGCCAAGTGGCCAGGCT
CTGAACTGGCTCTGGGCTCCTCCTCGTCTCTGCTTTAATCAGGACACCGTGAGGACAAGTGA
GGCCGTGAGTCTTGGTGTGATGCGGGGTGGGCTGGGCCGCTGGAGCCTCCGCCTGCTTCTC
CAGAAGACACGAATCATGACTCACGATTGCTGAAGCCTGAGCAGGTCTCTGTGGGCCGACCA
GAGGGGGGCTTCGAGGTGGTCCCTGGTACTGGGGTGACCGAGTGGACAGCCAGGGTGCAGC
TCTGCCCCGGGCTCGTGAAGCCTCAGATGTCCCAATCCAAGGGTCTGGAGGGGCTGCCGTGA
CTCCAGAGGCCTGAGGCTCCAGGGCTGGCTCTGGTGTTTACAAGCTGGACTCAGGGATCCTC
CTGGCCGCCCCGAGGGGGCTTGGAGGGCTGGACGGCAAGTCCGTCTAGCTCACGGGCCCT
CCAGTGGAATGGGTCTTTTCGGTGGAGATAAAAGTTGATTTGCTCTAACCGCAA

FIGURE 10

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56529
><subunit 1 of 1, 699 aa, 1 stop
><MW: 79553, pI: 7.83, NX(S/T): 0
MAACEGRRSGALGSSQSDFLTPPVGGAPWAVATTVMYPPPPPPHRDFISVTLSFGESYDN
SKSWRRRSCWRKWKQLSRLQRMILFLLAFLLFCGLLFYINLADHWKALAFRLEEEQKMRPE
IAGLKPANPPVLPAPQKADTDPENLPEISSQKTQRHIQRGPPHLQIRPPSQDLKDGTQEEAT
KRQEAPVDPRPEGDPQRTVISWRGAVIEPEQGTELPSRRAEVPTKPPLPPARTQGTPVHLNY
RQKGVIDVFLHAWKGYRKFAWGHDELKPVSRSFSEWFGLGLTLIDALDTMWILGLRKEFEEA
RKWVSKKLHFEKDVDVNLFESTITIRILGGLLSAYHLSGDSLFLRKAEDFGNRLMPAFRTPSKI
PYSDVNIGTGVAHPPRWTSDSTVAEVTISIQLFRELSRLTGDKKFQEAVEKVTQMIHGLSGK
KDGLVPMFINTHSGLFTHLGVFTL GARADSYEYLLKQWIQGGKQETQLLEDYVEAIEGVRT
HLLRHSEPSKLTFVGELAHGRFSAKMDHLVCFLPGTLALGVYHGLPASHMELAQELMETCYQ
MNRQMETGLSPEIVHFNLYPQPGRRDVEVKPADRHNLRLPETVESLFYLYRVTGDRKYQDWG
WEILQSFSRFRTRVPSGGYSSINNVQDPQKPEPRDKMESFFLGETLKYLFLLFSDDPNLLSLD
AYVFNTEAHPLPIWTPA
```

Important features of the protein:

Transmembrane domain:

amino acids 21-40 and 84-105 (type II)

FIGURE 11

GGCGCCGCGTAGGCCCCGGGAGGCCGGGCGGGCTGCGAGCGCCTGCCCCATGCGCCGC
CGCCTCTCCGCACGATGTTCCCCCTCGCGGAGGAAAGCGGCGCAGCTGCCCTGGGAGGACGGC
AGGTCCGGGTTGCTCTCCGGCGGCCTCCCTCGGAAGTGTTCCGTCTTCCACCTGTTGCTGGC
CTGCCTCTCGCTGGGCTTCTTCTCCCTACTCTGGCTGCAGCTCAGCTGCTCTGGGGACGTGG
CCCGGGCAGTCAGGGGACAAGGGCAGGAGACCTCGGGCCCTCCCCGTGCCTGCCCCCCAGAG
CCGCCCCCTGAGCACTGGGAAGAAGACGCATCCTGGGGCCCCCACC GCCTGGCAGTGCTGGT
GCCCTTCCGCGAACGCTTCGAGGAGCTCCTGGTCTTCGTGCCCCACATGCGCCGCTTCCTGA
GCAGGAAGAAGATCCGGCACCA CATCTACGTGCTCAACCAGGTGGACCACTTCAGGTTCAAC
CGGGCAGCGCTCATCAACGTGGGCTTCCTGGAGAGCAGCAACAGCACGGACTACATTGCCAT
GCACGACGTTGACCTGCTCCCTCTCAACGAGGAGCTGGACTATGGCTTTCTGAGGCTGGGC
CCTTCCACGTGGCCTCCCCGGAGCTCCACCCTCTCTACCACTACAAGACCTATGTCGGCGGC
ATCCTGCTGCTCTCCAAGCAGCACTACCGGCTGTGCAATGGGATGTCCAACCGCTTCTGGGG
CTGGGGCCGCGAGGACGACGAGTTCTACCGGCGCATTAAGGGAGCTGGGCTCCAGCTTTTCC
GCCCCCTCGGGAATCACA ACTGGGTACAAGACATTTTCGCCACCTGCATGACCCAGCCTGGCGG
AAGAGGGACCAGAAGCGCATCGCAGCTCAAAAAACAGGAGCAGTTCAAGGTGGACAGGGAGGG
AGGCCTGAACACTGTGAAGTACCATGTGGCTTCCCGCACTGCCCTGTCTGTGGGCGGGGCC
CCTGCACTGTCCTCAACATCATGTTGGACTGTGACAAGACCGCCACACCCTGGTGCACATTC
AGCTGAGCTGGATGGACAGTGAGGAAGCCTGTACCTACAGGCCATATTGCTCAGGCTCAGGA
CAAGGCCTCAGGTCGTGGGCCCAGCTCTGACAGGATGTGGAGTGGCCAGGACCAAGACAGCA
AGCTACGCAATTGCAGCCACCCGGCCGCCAAGGCAGGCTTGGGCTGGGCCAGGACACGTGGG
GTGCCTGGGACGCTGCTTGCCATGCACAGTGATCAGAGAGAGGCTGGGGTGTGTCCTGTCCG
GGACCCCCCTGCCTTCCTGCTCACCTACTCTGACCTCCTTCACGTGCCCAGGCCTGTGGG
TAGTGGGGAGGGCTGAACAGGACAACCTCTCATCACCTACTCTGACCTCCTTCACGTGCCC
AGGCCTGTGGGTAGTGGGGAGGGCTGAACAGGACAACCTCTCATCACCCCCAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 12

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56531

><subunit 1 of 1, 327 aa, 1 stop

><MW: 37406, pI: 9.30, NX(S/T): 1

MFPSRRKAAQLPWEDGRSGLLSGGLPRKCSVFHLFVACLSLGFFSLLWLQLSCSGDVARAVR
GQGQETSGPPRACPPEPPPEHWEEDASWGPHRLAVLVFPRERFEELLVFVPHMRRFLSRKKI
RHHIYVLNQVDHFRFNRAALINVGFLSSNSTDYIAMHDVDLLPLNEELDYGFPEAGPFHVA
SPELHPLYHYKTYVGGILLLSKQHYRLCNGMSNRFWGWGREDDFYRRIKGAGLQLFRPSGI
TTGYKTFRHLHDPAWRKRDQKRIAAQKQEQQFKVDREGGLNTVKYHVASRTALSVGGAPCTVL
NIMLDCDKTATPWCTFS

Signal peptide:

amino acids 1-42

Transmembrane domain:

amino acids 29-49 (type II)

N-glycosylation site.

amino acids 154-158

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 27-31

Tyrosine kinase phosphorylation site.

amino acids 226-233

N-myristoylation site.

amino acids 19-25, 65-71, 247-253, 285-291, 303-309, 304-310

FIGURE 13

CAATGTTTGCCTATCCACCTCCCCCAAGCCCCCTTACCTATGCTGCTGCTAACGCTGCTGCT
GCTGCTGCTGCTGCTTAAAGGCTCATGCTTGGAGTGGGGACTGGTCGGTGCCCAGAAAGTCT
CTTCTGCCACTGACGCCCCCATCAGGGATTGGGCCTTCTTTCCCCCTTCCTTTCTGTGTCTC
CTGCCTCATCGGCCTGCCATGACCTGCAGCCAAGCCCAGCCCCGTGGGGAAGGGGAGAAAGT
GGGGGATGGCTAAGAAAGCTGGGAGATAGGGAACAGAAGAGGGTAGTGGGTGGGCTAGGGGG
GCTGCCTTATTTAAAGTGGTTGTTTATGATTCTTATACTAATTTATACAAAGATATTAAGGC
CCTGTTTCATTAAGAAATTGTTCCCTTCCCCTGTGTTCAATGTTTGTAAGATTGTTCTGTGT
AAATATGTCTTTATAATAAACAGTTAAAAGCTGAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 14

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56862

<subunit 1 of 1, 73 aa, 1 stop

<MW: 7879, pI: 7.21, NX(S/T): 0

MLLLTLLLLLLLLLKGSCLWGLVGAQKVSSATDAPIRDWAFPPSFLCLLPHRPAMTCSQAQ
PRGEGEKVGDG

Important features:

Signal peptide:

amino acids 1-15

Growth factor and cytokines receptors family:

amino acids 3-18

FIGURE 15

GGGACCCATGCGGCCGTGACCCCCGGCTCCCTAGAGGCCAGCGCAGCCGCAGCGGACAAAG
GAGCATGTCCGCGCCGGGAAGGCCCGTCCCTCCGGCCGCCATAAGGCTCCGGTCGCCGCTGG
GCCCCGCGCCGCGCTCCTGCCCGCCCGGGCTCCGGGGCGGGCCCGCTAGGCCAGTGCGCCGCCG
CTCGCCCCGCAGGCCCCGGCCCCGCAGCATGGAGCCACCCGGACGCCGGCGGGGGCCGCGCGCA
GCCGCGCTGTTGCTGCCGCTCTCGCTGTTAGCGCTGCTCGCGCTGCTGGGAGGCGGCGGGCG
GCGGCGGCGCCGCGGCGCTGCCCGCCGGCTGCAAGCACGATGGGCGGCCCCGAGGGGCTGGC
AGGGCGGCGGGCGCCGCCGAGGGCAAGGTGGTGTGCAGCAGCCTGGAACCTCGCGCAGGTCCT
GCCCCCAGATACTCTGCCCAACCGCACGGTCACCCTGATTCTGAGTAACAATAAGATATCCG
AGCTGAAGAATGGCTCATTTTCTGGGTAAAGTCTCCTTGAAAGATTGGACCTCCGAAACAAT
CTTATTAGTAGTATAGATCCAGGTGCCTTCTGGGGACTGTCATCTCTAAAAAGATTGGATCT
GACAAACAATCGAATAGGATGTCTGAATGCAGACATATTTTCGAGGACTCACCAATCTGGTTC
GGCTAAACCTTTTCGGGGAATTTGTTTTCTTCATTATCTCAAGGAACTTTTGATTATCTTGCG
TCATTACGGTCTTTGGAATTCAGACTGAGTATCTTTTGTGTGACTGTAAACATACTGTGGAT
GCATCGCTGGGTAAAGGAGAAGAACATCACGGTACGGGATACCAGGTGTGTTTATCCTAAGT
CACTGCAGGCCCAACCAGTCACAGGCGTGAAGCAGGAGCTGTTGACATGCGACCCCTCCGCTT
GAATTGCCGTCTTTCTACATGACTCCATCTCATCGCCAAGTTGTGTTTGAAGGAGACAGCCT
TCCTTTCCAGTGCATGGCTTCATATATTGATCAGGACATGCAAGTGTTGTGGTATCAGGATG
GGAGAATAGTTGAAACCGATGAATCGCAAGGTATTTTTTGTGAAAAGAACATGATTCACAAC
TGCTCCTTGATTGCAAGTGCCCTAACCATTTCTAATATTCAGGCTGGATCTACTGGAAATTG
GGGCTGTCATGTCCAGACCAAACGTGGGAATAATACGAGGACTGTGGATATTGTGGTATTAG
AGAGTTCTGCACAGTACTGTCCTCCAGAGAGGGTGGTAAACAACAAAGGTGACTTCAGATGG
CCCAGAACATTGGCAGGCATTACTGCATATCTGCAGTGTACGCGGAACACCCATGGCAGTGG
GATATATCCCGGAAACCCACAGGATGAGAGAAAAGCTTGGCGCAGATGTGATAGAGGTGGCT
TTTGGGCAGATGATGATTATTCTCGCTGTCAGTATGCAAATGATGTCACTAGAGTTCTTTAT
ATGTTTAATCAGATGCCCCCTCAATCTTACCAATGCCGTGGCAACAGCTCGACAGTTACTGGC
TTACACTGTGGAAGCAGCCAACTTTTCTGACAAAATGGATGTTATATTTGTGGCAGAAATGA
TTGAAAAATTTGGAAGATTTACCAAGGAGGAAAAATCAAAAGAGCTAGGTGACGTGATGGTT
GACATTGCAAGTAACATCATGTTGGCTGATGAACGTGTCTGTGGCTGGCGCAGAGGGAAGC
TAAAGCCTGCAGTAGGATTGTGCAGTGTCTTCAGCGCATTGCTACCTACCGGCTAGCCGGTG
GAGCTCACGTTTATTCAACATATTCACCCAATATTGCTCTGGAAGCTTATGTCATCAAGTCT
ACTGGCTTCACGGGGATGACCTGTACCGTGTTCCAGAAAGTGGCAGCCTCTGATCGTACAGG
ACTTTTCGGATTATGGGAGGCGGGATCCAGAGGGAAACCTGGATAAGCAGCTGAGCTTTAAGT
GCAATGTTTCAAATACATTTTTCGAGTCTGGCACTAAAGGTATGTTACATTCTGCAATCATTT
AAGACTATTTACAGTTAAATTAGAATGCTCCAAATGTTCTGCTTCGCAAAATAACCTTATTA
AAAGATTTTTTTTTTGCAGGAAGATAGGTATTATTGCTTTTGCTACTGTTTTTAAAGAAACTA
ACCAGGAAGAACTGCATTACGACTTTCAAGGGCCCTAGGCATTTTTTGCCCTTGATTCCCTTT
CTTCACATAAAAATATCAGAAATTACATTTTATAACTGCAGTGGTATAAATGCAAATATACT
ATTGTTACATGTGAAAAAATTTTATTTGACTTAAAGTTTATTTATTTGTTTTTTTGCTCCT
GATTTTAAGACAATAAGATGTTTTTCATGGGCCCCCTAAAGTATCATGAGCCTTTGGCACTGC
GCCTGCCAAGCCTAGTGGAGAAGTCAACCCTGAGACCAGGTGTTTAATCAAGCAAGCTGTAT
ATCAAAATTTTTTGGCAGAAAACACAAATATGTCATATATCTTTTTTTTAAAAAAGTATTTCA
TTGAAGCAAGCAAAATGAAAGCATTTTTTACTGATTTTTTAAATTTGGTGCTTTAGATATATTT
GACTACACTGTATTGAAGCAAATAGAGGAGGCACAACTCCAGCACCCCTAATGGAACCACATT
TTTTTCACTTAGCTTTCTGTGGGCATGTGTAATTGTATTCTCTGCGGTTTTTAAATCTCACAG
TACTTTATTTCTGTCTTGTCCCTCAATAATATCACAAACAATATTCCAGTCATTTTAATGGC
TGCATAATAACTGATCCAACAGGTGTTAGGTGTTCTGGTTTAGTGTGAGCACTCAATAAATA
TTGAATGAATGAACGAAAAAAAAAAAAAAAAA

FIGURE 16

MEPPGRRRRGRAQPPLLLPLSLLALLALLGGGGGGGAAALPAGCKHDGRPRGAGRAAGAAEGK
VVCSSLELAQVLPPDTLPNRTVTLILSNKISELKNGSFSGLSLLERLDLRNNLISSIDPGA
FWGLSSLKRLDLTNNRIGCLNADIFRGLTNLVRNLNSGNLFSSLSQGTFDYLASLRSLEFQT
EYLLCDCNILWMHRWVKEKNITVRDTRCVYPKSLQAQPVTVGVKQELLTCDPPELPSFYMTF
SHRQVVFEGDSLPPFQCMASYIDQDMQVLWYQDGRIVETDESQGIFVEKNMIHNCSLIASALT
ISNIQAGSTGNWGCHVQTKRGNNTRTVDIVVLESSAQYCPPERVVNNKGDFRWPRTLGITA
YLQCTRNTHGSGIYPGNPQDERKAWRRCDRGGFWADDDYSRCQYANDVTRVLYMFNQMPNLN
TNAVATARQLLAYTVEAANFSDKMDVIFVAEMIEKFGRFTKEEKSKELGDMVDIASNIMLA
DERVLWLAQREAKACSRIVQCLQRIATYRLAGGAHVYSTYSPNIALEAYVIKSTGFTGMTCT
VFQKVAASDRTGLSDYGRRDPEGNLDKQLSFKCNVSNTFSSLALKVCYILQSFKTIYS

Signal peptide:

amino acids 1-33

Transmembrane domain:

amino acids 13-40 (type II)

N-glycosylation site.amino acids 81-85, 98-102, 159-163, 206-210, 301-305, 332-336,
433-437, 453-457, 592-596**N-myristoylation site.**amino acids 29-35, 30-36, 31-37, 32-38, 33-39, 34-40, 51-57,
57-63, 99-105, 123-129, 142-148, 162-168, 317-323, 320-326,
384-390, 403-409, 554-560

FIGURE 17

GCGTGGGGATGTCTAGGAGCTCGAAGGTGGTGCTGGGCCTCTCGGTGCTGCTGACGGCGGCC
ACAGTGGCCGGCGTACATGTGAAGCAGCAGTGGGACCAGCAGAGGCTTCGTGACGGAGTTAT
CAGAGACATTGAGAGGCAAATTCGGAAAAAGAAAACATTCGTCTTTTGGGAGAACAGATTA
TTTTGACTGAGCAACTTGAAGCAGAAAGAGAGAAGATGTTATTGGCAAAGGATCTCAAAA
TCATGACTTGAATGTGAAATATCTGTTGGACAGACAACACGAGTTTGTGTGTGTGTGTGTTGAT
GGAGAGTAGCTTAGTAGTATCTTCATCTTTTTTTTTTGGTCACTGTCCTTTTAACTTGATCA
AATAAAGGACAGTGGGTCATATAAGTTACTGCTTTCAGGGTCCCTTATATCTGAATAAAGGA
GTGTGGGCAGACACTTTTTGGAAGAGTCTGTCTGGGTGATCCTGGTAGAAGCCCCATTAGGG
TCACTGTCCAGTGCTTAGGGTTGTTACTGAGAAGCACTGCCGAGCTTGTGAGAAGGAAGGGA
TGGATAGTAGCATCCACCTGAGTAGTCTGATCAGTCGGCATGATGACGAAGCCAAGAGAACA
TCGACCTCAGAAGGACTGGAGGAAGGTGAAGTGGAGGGAGAGACGCTCCTGATCGTCGAATCC

FIGURE 18

MSRSSKVVVLGLSVLLTAATVAGVHVKQQWDQQRLRDGVIRDIERQIRKKENIRLLGEQIILT
EQLEAEREKMLLAKGSQKS

Signal peptide:

amino acids 1-21

FIGURE 19

CTGTCGTCTTTGCTTCAGCCGCAGTCGCCACTGGCTGCCTGAGGTGCTCTTACAGCCTGTTC
CAAGTGTGGCTTAATCCGTCTCCACCACCAGATCTTTCTCCGTGGATTCCCTCTGCTAAGACC
GCTGCCATGCCAGTGACGGTAACCCGCACCACCATCACAACCACCACGACGTCATCTTCGGG
CCTGGGGTCCCCCATGATCGTGGGGTCCCCTCGGGCCCTGACACAGCCCCTGGGTCTCCTTCGC
CTGCTGCAGCTGGTGTCTACCTGCGTGGCCTTCTCGCTGGTGGCTAGCGTGGGCGCCTGGAC
GGGGTCCATGGGCAACTGGTCCATGTTACCTGGTGCTTCTGCTTCTCCGTGACCCTGATCA
TCCTCATCGTGGAGCTGTGCGGGCTCCAGGCCCGCTTCCCCCTGTCTTGCGCAACTTCCCC
ATCACCTTCGCCTGCTATGCGGCCCTCTTCTGCCTCTCGGCCCTCCATCATCTACCCACCAC
CTATGTCCAGTTCCTGTCCCACGGCCGTTCGCGGGACCACGCCATCGCCGCCACCTTCTTCT
CCTGCATCGCGTGTGTGGCTTACGCCACCGAAGTGGCCTGGACCCGGGGCCCGGCCGGCGAG
ATCACTGGCTATATGGCCACCGTACCCGGGCTGCTGAAGGTGCTGGAGACCTTCGTTGCCTG
CATCATCTTCGCGTTCATCAGCGACCCCAACCTGTACCAGCACCAGCCGGCCCTGGAGTGGT
GCGTGGCGGTGTACGCCATCTGCTTCATCCTAGCGGCCATCGCCATCCTGCTGAACCTGGGG
GAGTGCACCAACGTGCTACCCATCCCCTTCCCCAGCTTCCTGTCGGGGCTGGCCTTGCTGTC
TGTCCTCCTCTATGCCACCGCCCTTGTTCTCTGGCCCCCTCTACCAGTTCGATGAGAAGTATG
GCGGCCAGCCTCGGCGCTCGAGAGATGTAAGCTGCAGCCGCAGCCATGCCTACTACGTGTGT
GCCTGGGACCGCCGACTGGCTGTGGCCATCCTGACGGCCATCAACCTACTGGCGTATGTGGC
TGACCTGGTGCACTCTGCCCACCTGGTTTTTGTCAAGGTCTTAAGACTCTCCCAAGAGGCTCC
CGTTCCCTCTCCAACCTCTTTGTTCTTCTTGCCCGAGTTTTCTTTATGGAGTACTTCTTTCC
TCCGCCTTTCCTCTGTTTTCTCTTCTCTGCTCTCCCCTCCCTCCACCTTTTTCTTTCCTTCC
CAATTCCTTGCACTCTAACCAGTTCCTGGATGCATCTTCTTCCCTTCCCTTTCCTCTTGCTGT
TTCCTTCCCTGTGTGTTTTGTTGCCCCACATCCTGTTTTACCCCTGAGCTGTTTCTCTTTTT
CTTTTCTTTCTTTTTTTTTTTTTTTTTTAAAGACGGATTCTCACTCTGTGGCCCAGGCTGGAG
TGCAGTGGTGCGATCTCAGCTCACTGCAACCCCCGCCTCCTGGGTTCAGCGATTCTCCTCC
CCCAGCCTCCCAAGTAGCTGGGAGGACAGGTGTGAGCTGCCGCACCCAGCCTGTTTCTCTTT
TTCCACTCTTCTTTTTTCTCATCTCTTTTCTGGGTGCTGTGCGCTTTCTTATCTGCCTGT
TTTGCAAGCACCTTCTCCTGTGTCCTTGGGAGCCCTGAGACTTCTTCTCTCCTTGCCTCCA
CCACCTCCAAAGGTGCTGAGCTCACATCCACACCCCTTGCAGCCGTCCATGCCACAGCCCC
CCAAGGGGCCCCATTGCCAAAGCATGCCTGCCACCCCTCGCTGTGCCTTAGTCAGTGTGTAC
GTGTGTGTGTGTGTGTGTTGGGGGGTGGGGGGTGGGTAGCTGGGGATTGGGCCCTCTTTCT
CCCAGTGGAGGAAGGTGTGCAGTGTACTTCCCCTTTAAATTAAAAACATATATATATAT
ATTTGGAGGTCAGTAATTTCCAATGGGCGGGAGGCATTAAGCACCGACCCTGGGTCCCTAGG
CCCCGCCTGGCACTCAGCCTTGCCAGAGATTGGCTCCAGAATTTTGGCCAGGCTTACAGAACAC
CCTAGCCTAGAGGCCATCTTAAAGGAAGCAGGGGCTGGATGCCTTTCATCCCAACTATTCT
CTGTGGTATGAAAAAG

FIGURE 20

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58727

<subunit 1 of 1, 322 aa, 1 stop

<MW: 35274, pI: 8.57, NX(S/T): 1

MPVTVTRTTITTTTSSSGLGSPMIVGSPRALTQPLGLLRLLQLVSTCVAFSLVASVGAWTG
SMGNWSMFTWCFCFSVTLLIILIVELCGLQARFPLSWRNFPITFACYAALFCLSASIIYPTY
VQFLSHGRSRDHAIAATFFSCIACVAYATEVAWTRARPGEITGYMATVPGLLKVLETFVACI
IFAFISDPNLYQHQPALWCVAVYAICFILAAIAILLNLGECTNVLPIPFPSFLSGLALLSV
LLYATALVLWPLYQFDEKYGQPRRSRDVSCSRSHAYYVCAWDRRLAVAILTAINLLAYVAD
LVHSAHLVFKV

Important features:**Transmembrane domains:**

amino acids 41-60 (type II), 66-85, 101-120, 137-153, 171-192,
205-226, 235-255 and 294-312

N-glycosylation site.

amino acids 66-69

Glycosaminoglycan attachment site.

amino acids 18-21

GAACGTGCCACCATGCCCAGCTAATTTTTGTATTTTGTAGTAGAGACGGGGTTTCACCATGTTGGCCAGGCTGGTC
TTGAACTCGTGACCTCATGATCCGCTCACCTCGGCCTCCCAAAGTGCTGGGATTACAGGCATGAGCCACTGACGC
CTGGCCAGCCTATGCATTTTTTAAGAAATTATTCTGTATTAGGTGCTGTGCTAAACATTGGGCCTACAGTGACCA
AAACAGACTGAATTTCCCAAGAGCCAAAGACCAGTGAGGGAGACCAACAAGAAACAGGAAATGCAAAAGAGACCA
TTATTACTCACTATGACTAAGGGTCACAAATGGGGTACGTTGATGGAGAGTGATTTGTTAAGAGACTACAGAGGG
AGGACAGACTACCAAGAGGGGGGGCCAGGAAAGCTCCTCTGACGAGGTGGTATTTTCAGCCCAAACCTGGAAGAATGA
GAAAGAGCTAGCCAGCCATCAGAATAGTCCAGAAGAGATGGGGAGCACTACACTCACTACACTTTGGCCCTGAGAA
AATAGCATGGGATTGGAGGAGGCTGGGGGAACACCACTTCTGCCGACCTGGGCAGGAGGCATTGAGGGCTTGAGA
AAGGGCAATGGCAGTAGCAGTAGAAAGGACAGGGTAGGAGCAGGGACTTTGCAGGTGGAATCATTAGGTCTTATC
AACAGATATGGGCAAGCAAAGCCAGGGGAGAATTGATGGTAATGCTGAGGTTTGGAGCCAGGCTAGATGGGACAG
TGGTGGGTGATGCAAAGGAAAGAGGTGAGGAAGCAGGGCCAGACGTGGGGAGAAGGTGTGGGGGTTTGGTTTCCA
TCTTGCCGAGTCTGCCGGAATGTGGATGGGAAGACCAAGAGGAGGAGCAAGGGGCAGAGGGGAAGGGAATCTTAA
AGAAGTCCTGGATGCCACACTCTTCTTCCTTCCTCCTCCTCCTCCTCCTCCTCAGAGGTCTCACTCGTGGTTCTTCAT
TTCCTGCCCTGCCCTCCATCTCCTCTGGGTGCTGGGAAAGTGGAGGATTAGCTGAAGTTTTCGTTCTCGGGGCCTG
TCTGAATCTCCATTGCTTTCTGGGAGGACATAATTCACCTGTCCTAGCTTCTTATCATCTTACATTTCCCTGTAG
CCACTGGGACATATGTGGTGTTCCTTCCTAGCTCCTGTCTCCTCCTCATGCCTTTGCTGGGTATGGGCATGTTAG
GGGGAAGGTCATTGCTGTCAGAGGGGCACTGACTTTCTAATGGTGTACCCAAAGGTGAATGTTGGAGACACAGTC
GCGATGCTGCCCAAGTCCCGGCGAGCCCTAACTATCCAGGAGATCGCTGCGCTGGCCAGGTCCTCCCTGCATGGT
ATGCAGCCCCCTCCCATGTTTTCTGGCCACTTTGTCTTTCTCCTCCCGTTTGCACATCCCTTTGGAAGTGTTCCT
GTGAGTACATGCTGGGGTCTCCCCCTTCTTCCTTGCTCAGGTGAATCTCAGCCCCCTTCTCCACCCAAAGGTTT
ACATGGATCCTAACTACTGCCACCCTTCCACCTCCCTGCACCTGTGCTCCCTGGCCTGGTCTTTTACCAGGCTTC
TCCACCCTCCCTATCTCCAGGTATTTCCAGGTGGTGAAGGACCACGTGACCAAGCCTACCGCCATGGCCCAGG
GCCGAGTGGCTCACCTCATTGAGTGAAGGGCTGGAGCAAGCCGAGTGACTCACCTGCTGCCCTGGAATCAGCCT
TTTCTCCTATTTCAGACCTCAGCGAGGGCGAACAAGAGGCTCGCTTTGCAGCAGGAGTGGCTGAGCAGTTTGCCA
TCGCGGAAGCCAAGCTCCGAGCATGGTCTTCGGTGGATGGCGAGGACTCCACTGATGACTCCTATGATGAGGACT
TTGCTGGGGGAATGGACACAGACATGGCTGGGCAGCTGCCCTGGGGCCGCACCTCCAGGACCTGTTTACCAGGCC
ACCGGTTCTCCCGGCTGTGCGCCAGGGCTCCGTGGAGCCTGAGAGCGACTGCTCACAGACCCTGTCCCCAGACA
CCCTGTGCTCTAGTCTGTGCAGCCTGGAGGATGGGTGTTGTTGGGCTCCCCGGCCCCGGCTGGCCTCCAGCTGCTGG
GCGATGAGCTGCTTCTCGCCAACTGCCCCCAGCCGGGAAAGTGCTTTCGCGAGCCTGGGCCCCACTGGAGGCC
AGGACTCACTCTACAACCTCGCCCCCTCACAGAGTCTGCTTTCCTCCCGCGGAGGAGGAGCCAGCCCCCTGCAAGG
ACTGCCAGCCACTCTGCCCACCCTAACGGGCAGCTGGGAACGGCAGCGGCAAGCCTCTGACCTGGCCTCTTCTG
GGGTGGTGTCTTAGATGAGGATGAGGCAGAGCCAGAGGAACAGTGAACCATCATGCCTGGCAGTGGCATGCA
TCCCCCGGCTGCTGCCAGGGGCAGAGCCTCTGTGCCCAAGTGTGGGCTCAAGGCTCCAGCAGAGCTCCACAGCC
TAGAGGGCTCCTGGGAGCGCTCGCTTCTCCGTTGTGTGTTTTGCATGAAAGTGTTTGGAGAGGAGGCAGGGGCTG
GGCTGGGGGCGCATGTCTGCCCCCACTCCCGGGGCTTGCCGGGGGTGCCCCGGGGCCTCTGGGGCATGGCTACA
GCTGTGGCAGACAGTGATGTTTATGTTCTTAAATGCCACACACATTTCTCCTCGGATAATGTGAACCTA
AGGGGGTTGTGACTGGGCTGTGTGAGGGTGGGGTGGGAGGGGGGCCAGCAACCCCCCACCCTCCCCATGCCTCTC
TCTTCTCTGCTTTTCTTCTCACTTCCGAGTCCATGTGCAGTGCTTGATAGAATACCCCCACCTGGAGGGGCTGG
CTCCTGCCCTCCCGGAGCCTATGGGTTGAGCCGTCCCTCAAGGGCCCCCTGCCAGCTGGGCTCGTGCTGTGCTTC
ATTCACCTCTCCATCGTCTCTAAATCTTCCTCTTTTTTCTTAAAGACAGAAGGTTTTTGGTCTGTTTTTTCAGTC
GGATCTTCTCTTCTGAGGCTTTTGAATGATGAAAGCATGTACCTCCACCCTTTTCTGGCCCCCTAATGG
GGCCTGGGGCCTTTCCCAACCCCTCCTAGGATGTGCGGGCAGTGTGCTGGCGCCTCACAGCCAGCCGGGCTGCC
ATTCACGCAGAGCTCTCTGAGCGGGAGGTGGAAGAAAGGATGGCTCTGGTTGCCACAGAGCTGGGACTTCATGTT
CTTCTAGAGAGGGCCACAAGAGGGCCACAGGGGTGGCCGGGAGTTGTCAGCTGATGCCCTGCTGAGAGGCAGGAAT
TGTGCCAGTGAGTGACAGTCATGAGGGAGTGTCTCTTCTTGGGGAGGAAAGAAGGTAGAGCCTTTCTGTCTGAAT
GAAAGGCCAAGGCTACAGTACAGGGCCCCGCCAGCCAGGGTGTTAATGCCACGTAGTGAGGCTCTGGCAG
ATCCTGCATTCCAAGGTCAGTGGACTGTACGTTTTTATGGTTGTGGGAAGGGTGGGTGGCTTTAGAATTAAGGGC
CTTGTAGGCTTTGGCAGGTAAGAGGGGCCAAGGTAAGAACGAGAGCCAACGGGCACAAGCATTCTATATATAAGT
GGCTCATTAGGTGTTTATTTTGTCTATTTAAGAATTTGTTTTATTAAATTAATATAAAAATCTTTGTAAATCTC
TAAAA

FIGURE 22

MFLATLSFLLPFAHPFGTVSCEYMLGSPLSSLAQVNLSPFVSHPKVHMDPNYCHPSTSLHLCS
LAWSFTRLLHPPLSPGISQVVKDHVTKPTAMAQGRVAHLIEWKGWSKPSDSPAALSAFSSY
SDLSEGEQEARFAAGVAEQFAIAEAKLRAWSSVDGEDSTDDSYDEDFAGGMDTDMAGQLPLG
PHLQDLFTGHRFSRPVRQGSVEPESDCSQTVSPDTLCSSLCSLEDGLLGSPARLASQLLGDE
LLLAKLPPSRESAFRSLGPLEAQDSLNSPLTESCLSPAEEEPAPCKDCQPLCPPLTGSWER
QRQASDLASSGVVSLDEDEAEPEEQ

Signal peptide:

amino acids 1-15

Casein kinase II phosphorylation site.

amino acids 123-127, 128-132, 155-159, 162-166, 166-170, 228-232,
285-289, 324-328

Tyrosine kinase phosphorylation site.

amino acids 44-52

N-myristoylation site.

amino acids 17-23, 26-32, 173-179

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 11-22

FIGURE 23

GGTTCCTGGGCGCTCTGTTACACAAGCAAGATACAGCCAGCCCCACCTAATTTTGTTTCCCT
GGCACCCCTCCTGCTCAGTGCGACATTGTCACACTTAACCCATCTGTTTTCTCTAATGCACGA
CAGATTCCTTTCAGACAGGACAACCTGTGATATTTTCAGTTCCTGATTGTAAATACCTCCTAAG
CCTGAAGCTTCTGTTACTAGCCATTGTGAGCTTCAGTTTCTTCATCTGCAAAATGGGCATAA
TACAATCTATTCTTGCCACATCAAGGGATTGTTATTCCTTTAAAAAAAACCAATACCAAAG
AAGCCTACAATGTTGGCCTTAGCCAAAATTCTGTTGATTTCAACGTTGTTTTATTCACTTCT
ATCGGGGAGCCATGGAAAAGAAAATCAAGACATAAACACAACACAGAACATTGCAGAAGTTT
TTAAAACAATGGAAAATAAACCTATTTCTTTGGAAAGTGAAGCAAACCTTAACTCAGATAAA
GAAAATATAACCACCTCAAATCTCAAGGCGAGTCATTCCCCTCCTTTGAATCTACCCAACAA
CAGCCACGGAATAACAGATTTCTCCAGTAACTCATCAGCAGAGCATTCTTTGGGCAGTCTAA
AACCCACATCTACCATTTCCACAAGCCCTCCCTTGATCCATAGCTTTGTTTCTAAAGTGCCT
TGGAATGCACCTATAGCAGATGAAGATCTTTTGCCCATCTCAGCACATCCCAATGCTACACC
TGCTCTGTCTTCAGAAAACCTTCACTTGGTCTTTGGTCAATGACACCGTGAAAACCTCCTGATA
ACAGTTCCATTACAGTTAGCATCCTCTCTTCAGAACCAACTTCTCCATCTGTGACCCCTTG
ATAGTGGAACCAAGTGGATGGCTTACCACAAACAGTGATAGCTTCACTGGGTTTACCCCTTA
TCAAGAAAAACAACCTCTACAGCCTACCTTAAAATTCACCAATAATTCAAACTCTTTCCAA
ATACGTCAGATCCCCAAAAGAAAATAGAAATACAGGAATAGTATTCGGGGCCATTTTAGGT
GCTATTCTGGGTGTCTCATTGCTTACTCTTGTGGGCTACTTGTTGTGTGGAAAAGGAAAAC
GGATTCATTTTCCCATCGGCGACTTTATGACGACAGAAATGAACCAGTTCTGCGATTAGACA
ATGCACCGGAACCTTATGATGTGAGTTTTGGGAATTCTAGCTACTACAATCCAACCTTTGAAT
GATTCAGCCATGCCAGAAAGTGAAGAAAATGCACGTGATGGCATTCTTATGGATGACATACC
TCCACTTCGTACTTCTGTATAGAACTAACAGCAAAAAGGCGTTAAACAGCAAGTGTCATCTA
CATCCTAGCCTTTTGACAAATTCATCTTTCAAAGGTTACACAAAATTACTGTCACGTGGAT
TTTGTCAAGGAGAATCATAAAAGCAGGAGACCAGTAGCAGAAATGTAGACAGGATGTATCAT
CCAAAGGTTTTCTTTCTTACAATTTTTGGCCATCCTGAGGCATTTACTAAGTAGCCTTAATT
TGTATTTTAGTAGTATTTTCTTAGTAGAAAATATTTGTGGAATCAGATAAAACTAAAAGATT
TCACCATTACAGCCCTGCCTCATAACTAAATAATAAAAATTATTCCACCAAAAATTCTAAA
ACAATGAAGATGACTCTTTACTGCTCTGCCTGAAGCCCTAGTACCATAATTCAAGATTGCAT
TTTCTTAAATGAAAATTGAAAGGGTGCTTTTTTAAAGAAAATTTGACTTAAAGCTAAAAAGAG
GACATAGCCCAGAGTTTCTGTTATTGGGAAATTGAGGCAATAGAAATGACAGACCTGTATTC
TAGTACGTTATAATTTTCTAGATCAGCACACACATGATCAGCCCCTGAGTTATGAAGCTGA
CAATGACTGCATTCAACGGGGCCATGGCAGGAAAGCTGACCCTACCCAGGAAAGTAATAGCT
TCTTTAAAAGTCTTCAAAGGTTTTGGGAATTTTAACTTGTCTTAATATATCTTAGGCTTCAA
TTATTTGGGTGCCTTAAAAACTCAATGAGAATCATGGT

FIGURE 24

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58732

><subunit 1 of 1, 334 aa, 1 stop

><MW: 36294, pI: 4.98, NX(S/T): 13

MLALAKILLISTLFYSLLSGSHGKENQDINTTQNI AEVFKTMENKPISLESEANLNSDKENI
TTSNLKASHSPPLNLPNNSHGITDFSSNSSAEHSLGSLKPTSTISTSPPLIHSFVSKVPWNA
PIADEDLLPISAHPNATPALSSNF TWSLVNDTVKTPDNSSITVSILSSEPTSPSVTPLIVE
PSGWLTTNSDSFTGFTPYQEKTTLQPTLKFTNNSKLFNPNTSDPQKENRNTGIVFGAILGAIL
GVSLTLVGYLLCGKRKTDSFSHRRLYDDRNEPVLRLDNAPEPYDV SFGNSSYYNPTLND SA
MPESEENARDGIPMDDIPPLRTSV

Signal peptide:

amino acids 1-23

Transmembrane domain:

amino acids 235-262

N-glycosylation site.

amino acids 30-34, 61-65, 79-83, 90-94, 148-152, 155-159,
163-167, 218-222, 225-229, 298-302, 307-311

FIGURE 25

AACAGGATCTCCTCTTGCAGTCTGCAGCCCAGGACGCTGATTCCAGCAGCGCCTTACCGCGC
AGCCCGAAGATTCACTATGGTGAAAATCGCCTTCAATACCCCTACCGCCGTGCAAAAGGAGG
AGGCGCGGCAAGACGTGGAGGCCCTCCTGAGCCGCACGGTCAGAACTCAGATACTGACCGGC
AAGGAGCTCCGAGTTGCCACCCAGGAAAAAGAGGGCTCCTCTGGGAGATGTATGCTTACTCT
CTTAGGCCTTTTCATTCATCTTGGCAGGACTTATTGTTGGTGGAGCCTGCATTTACAAGTACT
TCATGCCCAAGAGCACCATTTACCGTGGAGAGATGTGCTTTTTTTGATTCTGAGGATCCTGCA
AATTCCCTTCGTGGAGGAGAGCCTAACTTCCTGCCTGTGACTGAGGAGGCTGACATTCGTGA
GGATGACAACATTGCAATCATTGATGTGCCTGTCCCCAGTTTCTCTGATAGTGACCCTGCAG
CAATTATTCATGACTTTGAAAAGGGAATGACTGCTTACCTGGACTTGTTGCTGGGGAACTGC
TATCTGATGCCCCTCAATACTTCTATTGTTATGCCTCCAAAAAATCTGGTAGAGCTCTTTGG
CAAACCTGGCGAGTGGCAGATATCTGCCTCAAACCTTATGTGGTTCGAGAAGACCTAGTTGCTG
TGGAGGAAATTCGTGATGTTAGTAACCTTGGCATCTTTATTTACCAACTTTGCAATAACAGA
AAGTCCTTCCGCCTTCGTGCGCAGAGACCTCTTGCTGGGTTTCAACAAACGTGCCATTGATAA
ATGCTGGAAGATTAGACACTTCCCCAACGAATTTATTGTTGAGACCAAGATCTGTCAAGAGT
AAGAGGCAACAGATAGAGTGTCTTGGTAATAAGAAGTCAGAGATTTACAATATGACTTTAA
CATTAAAGGTTTATGGGATACTCAAGATATTTACTCATGCATTTACTCTATTGCTTATGCTTT
AAAAAAAGGAAAAAAAAAAAAAAAACTACTAACCCTGCAAGCTCTTGTCAAATTTTAGTTTAA
TGGCATTGCTTGTTTTTTTGAACTGAAATTACATGAGTTTCATTTTTTCTTTGCATTTATAG
GGTTTAGATTTCTGAAAGCAGCATGAATATATCACCTAACATCCTGACAATAAATCCATCC
GTTGTTTTTTTTGTTTGTTTGTTTTTTCTTTTCTTTAAGTAAGCTCTTTATTCATCTTATG
GTGGAGCAATTTTAAAATTTGAAATATTTTAAATTGTTTTTTGAACTTTTTGTGTAAAATATA
TCAGATCTCAACATTGTTGGTTTCTTTTGTTTTTTCATTTTGTACAACCTTTCTTGAATTTAGA
AATTACATCTTTGCAGTTCTGTTAGGTGCTCTGTAATTAACCTGACTTATATGTGAACAATT
TTCATGAGACAGTCATTTTTAACTAATGCAGTGATTCTTTCTCACTACTATCTGTATTGTGG
AATGCACAAAATTGTGTAGGTGCTGAATGCTGTAAGGAGTTTAGGTTGTATGAATTCTACAA
CCCTATAATAAATTTTACTCTATACAAAAAAAAAAAAAAAAAAAAA

FIGURE 26

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58828

<subunit 1 of 1, 263 aa, 1 stop

<MW: 29741, pI: 5.74, NX(S/T): 1

MVKIAFNTPTAVQKEEARQDVEALLSRTVRTQILTGKELRVATQEKEGSSSGRCMLTLLGLSF
ILAGLIVGGACIYKYFMPKSTIYRGEMCFFDSEDPANSLRGGEPNFLPVTEEADIREDDNIA
IIDVPVPSFSDSDPAAIHDFEKGMTAYLDLLLGNCYLMPLNTSIVMPPKNLVELFGKLASG
RYLPQTYVVREDLVAVEEIRDVSNLGIFIYQLCNNRKSFRLRRRDLLLGFNKRAIDKCWKIR
HFPNEFIVETKICQE

Type II transmembrane domain:

amino acids 53-75

N-glycosylation site.

amino acids 166-170

Casein kinase II phosphorylation site.

amino acids 35-39, 132-136, 134-138

N-myristoylation site.

amino acids 66-72, 103-109

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 63-74

FIGURE 27

GGAGGAGGGAGGGCGGGCAGGCGCCAGCCCAGAGCAGCCCCGGGCACCAGCACGGACTCTCT
CTTCCAGCCCAGGTGCCCCCACTCTCGCTCCATTCTGGCGGGAGCACCCAGTCCTGTACGCC
AAGGAACTGGTCCTGGGGGCACCAATGGTTTCGGCGGCAGCCCCCAGCCTCCTCATCCTTCTG
TTGCTGCTGCTGGGGTCTGTGCCTGCTACCGACGCCCCGCTCTGTGCCCTGAAGGCCACGTT
CCTGGAGGATGTGGCGGGTAGTGGGGAGGCCGAGGGCTCGTCCGGCCTCCTCCCCGAGCCTCC
CGCCACCCTGGACCCCCGGCCCTCAGCCCCACATCGATGGGGCCCCAGCCCACAACCCTGGGG
GGCCCATCACCCCCACCAACTTCCTGGATGGGATAGTGGACTTCTTCCGCCAGTACGTGAT
GCTGATTGCTGTGGTGGGCTCCCTGGCCTTTCTGCTGATGTTTCATCGTCTGTGCCGCGGTCA
TCACCCGGCAGAAGCAGAAGGCCTCGGCCTATTACCCATCGTCCTTCCCCAAGAAGAAGTAC
GTGGACCAGAGTGACCGGGCGGGGGCCCCCGGGCCTTCAGTGAGGTCCCCGACAGAGCCCC
CGACAGCAGGCCCCGAGGAAGCCCTGGATTCTTCCCGGCAGCTCCAGGCCGACATCTTGGCCG
CCACCCAGAACCTCAAGTCCCCCACCAGGGCTGCACTGGGCGGTGGGGACGGAGCCAGGATG
GTGGAGGGCAGGGGCGCAGAGGAAGAGGAGAAGGGCAGCCAGGAGGGGGACCAGGAAGTCCA
GGGACATGGGGTCCCAGTGGAGACACCAGAGGCGCAGGAGGAGCCGTGCTCAGGGGTCTTG
AGGGGGCTGTGGTGGCCGGTGAGGGCCAAGGGGAGCTGGAAGGGTCTCTCTTGTTAGCCCAG
GAAGCCCAGGGACCAGTGGGTCCCCCGAAAGCCCCTGTGCTTGACAGCAGTGTCCACCCCAG
TGTCTTAACAGTCCTCCCGGGCTGCCAGCCCTGACTGTCCGGCCCCCAAGTGGTCACCTCCCC
GTGTATGAAAAGGCCTTCAGCCCTGACTGCTTCCTGACACTCCCTCCTTGGCCTCCCTGTGG
TGCCAATCCCAGCATGTGCTGATTCTACAGCAGGCAGAAATGCTGGTCCCCGGTGCCCCGGA
GGAATCTTACCAAGTGCCATCATCCTTCACCTCAGCAGCCCCAAAGGGCTACATCCTACAGC
ACAGCTCCCCTGACAAAGTGAGGGAGGGCACGTGTCCCTGTGACAGCCAGGATAAAACATCC
CCCAAAGTGCTGGGATTACAGGCGTGAGCCACCGTGCCCGGCCCAAACACTACTTTTTTAAACA
GCTACAGGGTAAAATCCTGCAGCACCCACTCTGGAAAATACTGCTCTTAATTTTCTGAAGG
TGGCCCCCTGTTTCTAGTTGGTCCAGGATTAGGGATGTGGGGTATAGGGCATTTAAATCCTC
TCAAGCGCTCTCCAAGCACCCCCGGCCTGGGGGTGAGTTTCTCATCCCGCTACTGCTGCTGG
GATCAGGTTGAATGAATGGAACCTTCCTGTCTGGCCTCCAAAGCAGCCTAGAAGCTGAGGG
GCTGTGTTTGAGGGGACCTCCACCCTGGGGAAGTCCGAGGGGCTGGGGAAGGGTTTCTGACG
CCCAGCCTGGAGCAGGGGGGCCCTGGCCACCCCCTGTTGCTCACACATTGTCTGGCAGCCTG
TGTCACAAATATTCGTCAGTCCTCGACAGGGAGCCTGGGCTCCGTCTGCTTTAGGGAGGCT
CTGGCAGGAGGTCTCTCCCCCATCCCTCCATCTGGGGCTCCCCAACCTCTGCACAGCTCT
CCAGGTGCTGAGATATAATGCACCAGCACATAAACCTTTATTCCGGCCTGAAAAAAAAAAAA
AAGA

FIGURE 28

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58852

><subunit 1 of 1, 283 aa, 1 stop

><MW: 29191, pI: 4.52, NX(S/T): 0

MVSAAAPSLILLILLLLGSPATDARSVPLKATFLEDVAGSGEAEAGSSASSPSLPPPWTPAL
SPTSMGPQPTTLGGPSPPTNFLDGIVDFFRQYVMLIAVVGSLAFLLMFIVCAAVITRQKQKA
SAYYPSSFPPKKKYVDQSDRAGGPRAFSEVPDRAPDSRPEEALDSSRQLQADILAATQNLKSP
TRAALGGGDGARMVEGRGAEEEEKGSQEGDQEVQGHGVPVETPEAQEEPCSGVLEGAVVAGE
GQGELEGSLLLAQEAQGPVGPPEPCACSSVHPSV

Signal peptide:

amino acids 1-25

Transmembrane domain:

amino acids 94-118

N-myristoylation site.

amino acids 18-24, 40-46, 46-52, 145-151, 192-198, 193-199,
211-217, 238-244, 242-248

FIGURE 29

GTGGACTCTGAGAAGCCCAGGCAGTTGAGGACAGGAGAGAGAAGGCTGCAGACCCAGAGGGA
GGGAGGACAGGGAGTCGGAAGGAGGAGGACAGAGGAGGGCACAGAGACGCAGAGCAAGGGCG
GCAAGGAGGAGACCCTGGTGGGAGGAAGACACTCTGGAGAGAGAGGGGGCTGGGCAGAGATG
AAGTTCCAGGGGCCCTGGCCTGCCTCCTGCTGGCCCTCTGCCTGGGCAGTGGGGAGGCTGG
CCCCCTGCAGAGCGGAGAGGAAAGCACTGGGACAAATATTGGGGAGGCCCTTGGACATGGCC
TGGGAGACGCCCTGAGCGAAGGGGTGGGAAAGGCCATTGGCAAAGAGGCCGGAGGGGCAGCT
GGCTCTAAAGTCAGTGAGGCCCTTGGCCAAGGGACCAGAGAAGCAGTTGGCACTGGAGTCAG
GCAGGTTCCAGGCTTTGGCGCAGCAGATGCTTTGGGCAACAGGGTCGGGGAAGCAGCCCATG
CTCTGGGAAACACTGGGCACGAGATTGGCAGACAGGCAGAAGATGTCATTCGACACGGAGCA
GATGCTGTCCGCGGCTCCTGGCAGGGGGTGCTTGGCCACAGTGGTGCTTGGGAAACTTCTGG
AGGCCATGGCATCTTTGGCTCTCAAGGTGGCCTTGGAGGCCAGGGCCAGGGCAATCCTGGAG
GTCTGGGGACTCCGTGGGTCCACGGATACCCCGGAAACTCAGCAGGCAGCTTTGGAATGAAT
CCTCAGGGAGCTCCCTGGGGTCAAGGAGGCAATGGAGGGCCACCAAACCTTTGGGACCAACAC
TCAGGGAGCTGTGGCCAGCCTGGCTATGGTTCAGTGAGAGCCAGCAACCAGAATGAAGGGT
GCACGAATCCCCCACCATCTGGCTCAGGTGGAGGCTCCAGCAACTCTGGGGGAGGCAGCGGC
TCACAGTCGGGCAGCAGTGGCAGTGGCAGCAATGGTGACAACAACAAATGGCAGCAGCAGTGG
TGGCAGCAGCAGTGGCAGCAGCAGTGGCAGCAGCAGTGGCGGCAGCAGTGGCGGCAGCAGTG
GTGGCAGCAGTGGCAACAGTGGTGGCAGCAGAGGTGACAGCGGCAGTGAGTCCTCCTGGGGA
TCCAGCACCGGCTCCTCCTCCGGCAACCACGGTGGGAGCGGCGGAGGAAATGGACATAAACC
CGGGTGTGAAAAGCCAGGGAATGAAGCCCGCGGGAGCGGGGAATCTGGGATTCAGGGCTTCA
GAGGACAGGGAGTTTCCAGCAACATGAGGGAAATAAGCAAAGAGGGCAATCGCCTCCTTGGA
GGCTCTGGAGACAATTATCGGGGGCAAGGGTCGAGCTGGGGCAGTGGAGGAGGTGACGCTGT
TGGTGGAGTCAATACTGTGAACTCTGAGACGTCTCCTGGGATGTTTAACTTTGACACTTTCT
GGAAGAATTTTAAATCCAAGCTGGGTTTCATCAACTGGGATGCCATAAACAAGGACCAGAGA
AGCTCTCGCATCCCGTGACCTCCAGACAAGGAGCCACCAGATTGGATGGGAGCCCCCACA
CCCTCCTTAAACACCAACCCTCTCATCTAATCTCAGCCCTTGCCCTTGAAATAAACCTTA
GCTGCCCCACAA
AAA

FIGURE 30

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA59212

><subunit 1 of 1, 440 aa, 1 stop

><MW: 42208, pI: 6.36, NX(S/T): 1

MKFQGPLACLLLLALCLGSGEAGPLQSGEESTGTNIGEALGHGLGDALSEGVGKAIGKEAGGA
AGSKVSEALGQGTREAVGTGVRQVPFGAADALGNRVGEAAHALGNTGHEIGRQAEDVIRHG
ADAVRGSWQGVPGHSGAWETSGGHGIFGSQGGGLGGQGGQGNPGGLGTPWVHGYPGNSAGSFGM
NPQGAPWGQGGNGGPPNFGTNTQGAVAQPGYGSVRASNQNEGCTNPPPSGSGGGSSNSGGGS
GSQSGSSSGSGSNGDNNNGSSSSGGSSSSGGSSSSGGSSSGSGSSGSGSGNSGGSRGDSGSESSW
GSSTGSSSGNHGGSGGGNGHKPGCEKPGNEARGSGESGIQGFRGQGVSSNMREISKEGNRLL
GGSGDNYRGQGSSWGSGGDAVGGVNTVNSETSPGMFNFDTFWKNFKSKLGFINWDAINKDQ
RSSRIP

Signal peptide:

amino acids 1-21

N-glycosylation site.

amino acids 265-269

Glycosaminoglycan attachment site.

amino acids 235-239, 237-241, 244-248, 255-259, 324-328, 388-392

Casein kinase II phosphorylation site.

amino acids 26-30, 109-113, 259-263, 300-304, 304-308

N-myristoylation site.

amino acids 17-23, 32-38, 42-48, 50-56, 60-66, 61-67, 64-70,
74-80, 90-96, 96-102, 130-136, 140-146, 149-155, 152-158,
155-161, 159-165, 163-169, 178-184, 190-196, 194-200, 199-205,
218-224, 236-242, 238-244, 239-245, 240-246, 245-251, 246-252,
249-252, 253-259, 256-262, 266-272, 270-276, 271-277, 275-281,
279-285, 283-289, 284-290, 287-293, 288-294, 291-297, 292-298,
295-301, 298-304, 305-311, 311-317, 315-321, 319-325, 322-328,
323-329, 325-331, 343-349, 354-360, 356-362, 374-380, 381-387,
383-389, 387-393, 389-395, 395-401

Cell attachment sequence.

amino acids 301-304

FIGURE 31

GACCGGTCCCTCCGGTCCTGGATGTGCGGACTCTGCTGCAGCGAGGGCTGCAGGCCCGCCGGGCGGTGCTCACCG
TGCCCTGGCTGGTGGAGTTTCTCTCCTTTGCTGACCATGTTGTTCCCTTGCTGGAATATTACCGGGACATCTTCA
CTCTCCTGCTGCGCCTGCACCGGAGCTTGGTGTGTCGCGAGGAGAGTGAGGGGAAGATGTTGTTTCTGAACAAGC
TGCTGCTACTTGCTGTCCTGGGCTGGCTTTTCCAGATTCCCACAGTCCCTGAGGACTTGTCTTTCTGGAAGAGG
GTCCCTCATATGCCTTTGAGGTGGACACAGTAGCCCCAGAGCATGGCTTGGACAATGCGCCTGTGGTGGACCAGC
AGCTGCTCTACACCTGCTGCCCCCTACATCGGAGAGCTCCGGAAGTGTGCTGCTTCGTGGGTGTGAGGCAGTAGTG
GACGGAGTGGGGGCTTCATGAGGAAAATCACCCCCACCACTACCACCAGCCTGGGAGCCCAGCCTTCCCAGACCA
GCCAGGGGCTGCAGGCACAGCTCGCCCAGGCCTTTTCCACAACCAGCCGCCCTCCTTGCGCCGGACCGTAGAGT
TCGTGGCAGAAAGAATTGGATCAAACCTGTGTCAAACATATCAAGGCTACACTGGTGGCAGATCTGGTGGCCAGG
CAGAGTCACCTTCTCAAGAGCAGCTGGTGACACAGGGAGAGGAAGGGGGAGACCCAGCCCAGCTGTTGGAGATCT
TGTGTTCCCAGCTGTGCCCTCACGGGGCCCAGGCATTGGCCCTGGGGCGGGAGTTCTGTCAAAGGAAGAGCCCTG
GGGCTGTGCGGGCGCTGCTTCCAGAGGAGACCCCGGCAGCCGTTCTGAGCAGTGCAGAGAACATTGCTGTGGGGC
TTGCAACAGAGAAAGCCTGTGCTTGGCTGTGAGCCAAACATCACAGCACTGATCAGGAGGGAGGTGAAAGCAGCAG
TGAGTCGCACACTTCGAGCCCAGGGTCCTGAACCTGCTGCCCCGGGGGGAGCGGAGGGGCTGCTCCCGCGCCTGAC
GTGCTCTCCTTGGCCGTGGGGCCACGGGACCCTGACGAGGGAGTCTCCCCAGAGCATCTGGAACAGCTCCTAGGC
CAGCTGGGCCAGACGCTGCGGTGCCGCCAGTTCTGTGCCACCTGCTGAGCAGCATCTGGCAAAGTGCTCTGTG
GAGTTAGCTTCCCTCCTCGTTGCAGATCAAATTCCTATCCTAGGGCCCCCGGCACAGTACAGGCTGGAGAGAGGG
CAGGCTCGAAGGCTTCTGCACATGCTGCTTTCTTGTGGAAGGAAGACTTTCAGGGGCCGGTTCCGCTGCAGCTG
CTGCTGAGCCCAAGAAATGTGGGGCTTCTGGCAGACACAAGGCCAAGGGAGTGGGACTTGCTGCTATTCTTGCTA
CGGGAGCTGGTGGAGAAGGGTCTGATGGGACGGATGGAGATAGAGGCCTGCCTGGGCAGCCTCCACCAGGCCCAG
TGGCCAGGGGACTTTGCTGAAGAATTAGCAACACTGTCTAATCTGTTTCTAGCCGAGCCCCACCTGCCAGAACCC
CAGCTAAGAGCCTGTGAGTTGGTGCAGCCAAACCGGGGCACTGTGCTGGCCCAGAGCTAGGGCTGAGAAGTGGCC
CTGCCCTTGGGCATTGCACCAGAACCCTGGACCCCCGCCTCACGAGGAGGCCCAAGTGCCCAATGCAGACCCTCAC
TGGTTGGGGTGTAGCTGGGTCTACAGTCAGACTTCTGTCTAAGGGTGTCACTGCCTGGCATCCCACCACGCGA
ATCCTAGAGGAAGGAGAGTTGGCCTGATTTGGGATTATGGCAGAAAAGTCCAGAGATGCCAGTCTTGGAGTAGAA
GAGGTGGTGTGTTTATCTCTTGGATACTAAATGAAATGAGGTGTGTGGGCTTGTCAACACAGAATTCAAGCCT
CATTGCTATCCCAGCATCTCTTAAACTTTGTAGTCTTGGAAATTCATGACAGAGGCAAATGACTCCTGCTTAAC
TTATGAAGAAAGTTAAACATGAATCTTGGGAGTCTACATTTTCTTATCACAGGAGCTGGACTGCCATCTCCTT
ATAAATGCCTAACACAGGCCGGGTCTGGTGGCTCATGCCTGTAATCCCAGCACTTTGAGAGGCCTGAGGTGCGCG
GACTGCCTGAGGTGAGGAATTCAAGACCAGCCTGGCCAACATGGCAAAACCCCATCTCTACTAAAAATAAAAAA
TTATTAGCTGGGCATGGTGGTGTGTGCTGTAATCCCAGCTACTCAGGAGGATGAGGCAGGAGACCTGCTTGAAC
CTGGAGGTGGAGGTGTCAGTGAGCCGAGGTGCGACCACTGCCTCCAGTCTGGGTAACAGAGCGAGACTTTCTAG
AAAAAGCCTAACAAACAGATAAGGTAGGACTCAACCAACTGAAACCTGACTTTCCCCCTGTACCTTCAGCCCCTG
TGCAGGTAGTAACCTCTTGAGACCTCTCCCTGACCAGGGACCAAGCACAGGGCATTTAGAGCTTTTTAGATAAAA
CTGGTTTTCTTTAAAAAAGGGGCTTTTATTAAATCTCCCCACACGATGGCTCCTGCAATCTGCCACAGCTC
TTTTTTTTTTTTTTTTTAAAAAGGGCTTTTATTAAATCTCCCCACACGATGGCTCCTGCAATCTGCCACAGCTC
TGGGGCGTGTCTGTAGGGAAAGGCCCTGTTTTCCCTGAGGCGGGGCTGGGCTTGTCCATGGGTCCGCGGAGCTG
GCCGTGCTTGGCGCCCTGGCGTGTGTCTAGCTGCTTCTTGCCGGGCACAGAGCTGCGGGGTCTGGGGGCACCGGG
AGCTAAGAGCAGGCTCTGGTGCAGGGGTGGAGGCCTGTCTCTTAACCGACACCCTGAGGTGCTCCTGAGATGCTG
GGTCCACCCTGAGTGGCACGGGGAGCAGCTGTGGCCGGTGTCTCCTTCYTAGGCCAGTCTGGGGAACTAAGCTC
GGGCCCTTCTTTGCAAAGACCGAGGATGGGGTGGGTGTGGGGGACTCATGGGGAATGGCCTGAGGAGCTACGTGT
GAAGAGGGCGCCGGTTTGTGCTGTCAGCGGCCTGGAGCGCCTCTCTCCTGAGCCTCAGTTTCCCTTTCCGTCTA
ATGAAGAACATGCCGTCTCGGTGTCTCAGGGCTATTAGGACTTGCCCTCAGGAAGTGGCCTTGGACGAGCGTCAT
GTTATTTTCACAACTGTCTGCGACGTTGGCCTGGGCACGTGATGGAATGGCCCATGTCCCTCTGCTGCGTGGAC
GTCGCGGTGCGGAGTGCGCAGCCAGAGGCGGGGCCAGACGTGCGCCTGGGGGTGAGGGGAGGCGCCCCGGGAGGG
CCTCACAGGAAGTTGGGCTCCCGCACCAACAGGCAGGGCGGGCTCCCGCCGCGCCGCGCCACCAACCGTCCAGG
GGCCGGTAGACAAAGTGGAAGTCGCGCTTGGGCTGCTGCGCAGCAGGTAGCCCTTGATGCAGTGCGGCAGCGCG
TCGTCCGCCAGCTGGAAGCAGCGCCCGTCCACCAGCACGAACAGCCGGTGCCT

FIGURE 32

MCFLNKLLLLLAVLGWLFQIPTVPEDLFFLEEGPSYAFEVDTVAPDHGLDNAPVVDQQLLYTC
CPYIGELRKLLASWVSGSSGRSGGFMRKITPTTTTSLGAQPSQTSQGLQAQLAQAFFHNQPP
SLRRTVEFVAERIGSNCVKHIKATLVADLVRQAESLLQEQLVTQGEEGDPAQLLEILCSQL
CPHGAQALALGREFCQRKSPGAVRALLPEETPAAVLSSAENIAVGLATEKACAWLSANITAL
IRREVKAASRTTLRAQGPEPAARGERRGCSRA

Signal peptide:

amino acids 1-18

N-glycosylation site.

amino acids 244-248

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 89-93

Casein kinase II phosphorylation site.

amino acids 21-25, 167-171, 223-227

N-myristoylation site.

amino acids 100-106, 172-178, 207-213

Microbodies C-terminal targeting signal.

amino acids 278-282

FIGURE 33

TCCCTTGACAGGTCTGGTGGCTGGTTCGGGGTCTACTGAAGGCTGTCTTGATCAGGAACTG
AAGACTCTCTGCTTTTGCCACAGCAGTTCCTGCGAGCTTCCTTGAGGTGTGAACCCACATCCC
TGCCCCCAGGGCCACCTGCAGGACGCCGACACCTACCCCTCAGCAGACGCCGGAGAGAAATG
AGTAGCAACAAAGAGCAGCGGTGAGCAGTGTTTCGTGATCCTCTTTGCCCTCATCACCATCCT
CATCCTCTACAGCTCCAACAGTGCCAATGAGGTCTTCCATTACGGCTCCCTGCGGGGCCGTA
GCCGCCGACCTGTCAACCTCAAGAAGTGGAGCATCACTGACGGCTATGTCCCCATTCTCGGC
AACAAGACACTGCCCTCTCGGTGCCACCAGTGTGTGATTGTGTCAGCAGCTCCAGCCACCTGCT
GGGCACCAAGCTGGGCCCTGAGATCGAGCGGGCTGAGTGTACAATCCGCATGAATGATGCAC
CCACCACTGGCTACTCAGCTGATGTGGGCAACAAGACCACCTACCGCGTCGTGGCCCATTC
AGTGTGTTCCGCGTGCTGAGGAGGCCCCAGGAGTTTGTCAACCGGACCCCTGAAACCGTGTT
CATCTTCTGGGGGCCCCCGAGCAAGATGCAGAAGCCCCAGGGCAGCCTCGTGCGTGTGATCC
AGCGAGCGGGCCTGGTGTTCCTCAACATGGAAGCATATGCCGTCTCTCCCGGCCGCATGCCG
CAATTTGACGACCTCTTCCGGGGTGAGACGGGCAAGGACAGGGAGAAGTCTCATTCGTGGTT
GAGCACAGGCTGGTTTACCATGGTGATCGCGGTGGAGTTGTGTGACCACGTGCATGTCTATG
GCATGGTCCCCCCCCAACTACTGCAGCCAGCGGCCCCGCCTCCAGCGCATGCCCTACCCTAC
TACGAGCCCAAGGGGCCGACGAATGTGTACCTACATCCAGAATGAGCACAGTCGCAAGGG
CAACCACCACCGCTTCATCACCGAGAAAAGGGTCTTCTCATCGTGGGCCAGCTGTATGGCA
TCACCTTCTCCCACCCCTCCTGGACCTAGGCCACCCAGCCTGTGGGACCTCAGGAGGGTCAG
AGGAGAAGCAGCCTCCGCCAGCCGCTAGGCCAGGGACCATCTTCTGGCCAATCAAGGCTTG
CTGGAGTGTCTCCAGCCAATCAGGGCCTTGAGGAGGATGTATCCTCCAGCCAATCAGGGCC
TGGGGAATCTGTTGGCGAATCAGGGATTGAGGAGTCTATGTGGTTAATCAGGGGTGTCTTTC
TTGTGCAGTCAGGGTCTGCGCACAGTCAATCAGGGTAGAGGGGGTATTTCTGAGTCAATCTG
AGGCTAAGGACATGTCCTTTCCCATGAGGCCTTGGTTCAGAGCCCCAGGAATGGACCCCCCA
ATCACTCCCCACTCTGCTGGGATAATGGGGTCTGTCCCAAGGAGCTGGGAACTTGGTGTG
CCCCCTCAATTTCCAGCACCAGAAAGAGAGATTGTGTGGGGGTAGAAGCTGTCTGGAGGCC
GGCCAGAGAAATTTGTGGGGTTGTGGAGGTTGTGGGGGCGGTGGGGAGGTCCCAGAGGTGGGA
GGCTGGCATCCAGGTCTTGGCTCTGCCCTGAGACCTTGGACAAACCCTTCCCCCTCTCTGGG
CACCTTCTGCCCACACCAGTTTCCAGTGCGGAGTCTGAGACCCTTTCCACCTCCCCTACAA
GTGCCCTCGGGTCTGTCTCCCCGTCTGGACCTCCCAGCCACTATCCCTTGCTGGAAGGCT
CAGCTCTTTGGGGGGTCTGGGGTGACCTCCCCACCTCCTGGAAACTTTAGGGTATTTTTGC
GCAAACTCCTTCAGGGTTGGGGGACTCTGAAGGAAACGGGACAAAACCTTAAGCTGTTTTCT
TAGCCCCCTCAGCCAGCTGCCATTAGCTTGGCTCTTAAAGGGCCAGGCCTCCTTTTCTGCCCT
CTAGCAGGGAGGTTTTCCAACGTGTTGGAGGCGCCTTTGGGGCTGCCCTTTGTCTGGAGTCA
CTGGGGGCTTCCGAGGGTCTCCCTCGACCCTCTGTCTGCTGGGATGGCTGTCTGGGAGCTGT
ATCACCTGGGTTCTGTCCCCTGGCTCTGTATCAGGCACTTTATTAAAGCTGGGCCTCAGTGG
GGTGTGTTTGTCTCCTGCTCTTCTGGAGCCTGGAAGGAAAGGGCTTCAGGAGGAGGCTGTGA
GGCTGGAGGGACCAGATGGAGGAGGCCAGCAGCTAGCCATTGCACACTGGGGTGATGGGTGG
GGGCGGTGACTGCCCCAGACTTGGTTTTGTAAATGATTTGTACAGGAATAAACACACCTACGC
TCCGGAAA

FIGURE 34

MSSNKEQRS AVFVILFALITILILYSSNSANEVFHYGSLRGRSRRPVNLKKWSITDGYVPIL
GNKTLPSRCHQCIVIVSSSSHLLGTKLGPEIERAECTIRMNDAPTTGYSADVGNKTTYRVVAH
SSVFRVLRRPQEFVNRTPETVFIWGPSPKMQKPQGSLVRVIQRAGLVFPNMEAYAVSPGRM
RQFDDLFRGETGKDREKSHSWLSTGWFTMVI AVELCDHVHVYGMVPPNYCSQRPRLQRMPIYH
YYEPKGPDECVTYIQNEHSRKGNHHRFITEKRVFSSWAQLYGITFSHPSWT

Signal peptide:

amino acids 1-29

Transmembrane domain:

amino acids 9-31 (type II)

N-glycosylation site.

amino acids 64-68, 115-119

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 50-54

Casein kinase II phosphorylation site.

amino acids 3-7, 29-33, 53-57, 197-201

Tyrosine kinase phosphorylation site.

amino acids 253-262

N-myristoylation site.

amino acids 37-43, 114-120, 290-294

FIGURE 35

GTTTCTCATAGTTGGCGTCTTCTAAAGGAAAAACACTAAAATGAGGAACTCAGCGGACCGGGAGCGACGCAGCTT
GAGGGAAGCATCCCTAGCTGTTGGCGCAGAGGGGCGAGGCTGAAGCCGAGTGGCCCCGAGGTGTCTGAGGGGCTGG
GGCAAAGGTGAAAGAGTTTCAGAACAAAGCTTCCTGGAACCCATGACCCATGAAGTCTTGTGACATTTATACCGT
CTGAGGGTAGCAGCTCGAAACTAGAAGAAGTGGAGTGTGTCAGGGACGGCAGTATCTCTTTGTGTGACCCTGGC
GGCCTATGGGACGTTGGCTTCAGACCTTTGTGATACACCATGCTGCGTGGGACGATGACGGCGTGGAGAGGAATG
AGGCCTGAGGTCACACTGGCTTGCTCCTCCTAGCCACAGCAGGCTGCTTTGCTGACTTGAACGAGGTCCCTCAG
GTCACCGTCCAGCCTGCGTCCACCGTCCAGAAGCCCCGAGGCACTGTGATCTTGGGCTGCGTGGTGGAAACCTCCA
AGGATGAATGTAACCTGGCGCCTGAATGGAAAGGAGCTGAATGGCTCGGATGATGCTCTGGGTGTCTCATCACC
CACGGGACCCCTCGTCATCACTGCCCTTAACAACCACACTGTGGGACGGTACCAGTGTGTGGCCCCGATGCCTGCG
GGGGCTGTGGCCAGCGTGCCAGCCACTGTGACACTAGCCAATCTCCAGGACTTCAAGTTAGATGTGCAGCAGCTG
ATTGAAGTGGATGAGGGAAACACAGCAGTCAATTGCCTGCCACCTGCCTGAGAGCCACCCCAAAGCCCCAGGTCCGG
TACAGCGTCAAACAAGAGTGGCTGGAGGCCTCCAGAGGTAACCTGATCATGCCCTCAGGGAACCTCCAGATT
GTGAATGCCAGCCAGGAGGACGAGGGCATGTACAAGTGTGCAGCCTACAACCCAGTGACCCAGGAAGTGAACACC
TCCGGCTCCAGCGACAGGCTACGTGTGCGCCGCTCCACCGCTGAGGCTGCCCGCATCATCTACCCCCCAGAGGCC
CAAACCATCATCGTCACCAAAGGCCAGAGTCTCATTCTGGAGTGTGTGGCCAGTGGAAATCCACCCCCACGGGTC
ACCTGGGCCAAGGATGGGTCCAGTGTACCGGCTACAACAAGACGCGCTTCTGCTGAGCAACCTCCTCATCGAC
ACCACGAGCGAGGAGGACTCAGGCACCTACCGCTGCATGGCCGACAATGGGGTTGGGCAGCCCCGGGGCAGCGGTC
ATCCTCTACAATGTCCAGGTGTTTGAACCCCCCTGAGGTCAACCATGGAGCTATCCCAGCTGGTCATCCCCCTGGGGC
CAGAGTGCCAAGCTTACCTGTGAGGTGCGTGGGAACCCCCCGCCCTCCGTGCTGTGGCTGAGGAATGCTGTGCCC
CTCATCTCCAGCCAGCGCCTCCGGCTCTCCCGCAGGGGCCCTGCGCGTGTCTCAGCATGGGGCCTGAGGACGAAGGC
GTCTACCAAGTGCATGGCCGAGAACGAGGTTGGGAGCGCCCATGCCGTAGTCCAGCTGCGGACCTCCAGGCCAAGC
ATAACCCCAAGGCTATGGCAGGATGCTGAGCTGGCTACTGGCACACCTCCTGTATCACCTCCAAACTCGGCAAC
CCTGAGCAGATGCTGAGGGGGCAACCGGCGCTCCCCAGACCCCAACGTCAGTGGGGCCTGCTTCCCCGAAGTGT
CCAGGAGAGAAGGGGCAGGGGGCTCCCGCCGAGGCTCCCATCATCCTCAGCTCGCCCCGCACCTCCAAGACAGAC
TCATATGAACCTGGTGTGGCGGCTCGGCATGAGGGCAGTGGCCGGGCGCCAATCCTCTACTATGTGGTGAAACAC
CGCAAGCAGGTACAAATTCCTCTGACGATTGGACCATCTCTGGCATTCCAGCCAACCAGCACCAGCTGACCTC
ACCAGACTTGACCCCGGGAGCTTGTATGAAGTGGAGATGGCAGCTTACAACGTGCGGGGAGAGGGCCAGACAGCC
ATGGTCACCTTCCGAACCTGGACGGCGGCCCAACCCGAGATCATGGCCAGCAAAGAGCAGCAGATCCAGAGAGAC
GACCCTGGAGCCAGTCCCCAGAGCAGCAGCCAGCCAGACCAGGCGCCTCTCCCCCCAGAAGCTCCCGACAGG
CCCACCATCTCCACGGCCTCCGAGACCTCAGTGTACGTGACCTGGATTCCCCGTGGGAATGGTGGGTTCCTAATC
CAGTCCTTCCGTGTGGAGTACAAGAAGCTAAAGAAAGTGGGAGACTGGATTCTGGCCACCAGCGCCATCCCCCA
TCGCGGCTGTCCGTGGAGATCACGGGCCTAGAGAAAGGCACCTCCTACAAGTTTCGAGTCCGGGCTCTGAACATG
CTGGGGGAGAGCGAGCCAGCGCCCCCTCTCGGCCCTACGTGGTGTGCGGCTACAGCGGTGCGGTGTACGAGAGG
CCCGTGGCAGGTCTTATATCACCTTCACGGATGCGGTCAATGAGACCACCATCATGCTCAAGTGGATGTACATC
CCAGCAAGTAACAACAACACCCCAATCCATGGCTTTTATATCTATTATCGACCCACAGACAGTGACAATGATAGT
GACTACAAGAAGGATATGGTGGAAAGGGGACAAGTACTGGCACTCCATCAGCCACCTGCAGCCAGAGACCTCCTAC
GACATTAAGATGCAGTGCTTCAATGAAGGAGGGGAGAGCGAGTTCAGCAACGTGATGATCTGTGAGACCAAGCT
CGGAAGTCTTCTGGCCAGCCTGGTGCAGTGCACCCCCCACTCTGGCCCCACACAGCCGCCCCCTTCTGAAACC
ATAGAGCGGCGGTGGGCACTGGGGCCATGGTGGCTCGCTCCAGCGACCTGCCCTATCTGATTGTGCGGGTCTGTC
CTGGGCTCCATCGTTCTCATCATCGTCACCTTCATCCCCCTCTGCTTGTGGAGGGCCTGGTCTAAGCAAAAACAT
ACAACAGACCTGGGTTTTCTCGAAGTGCCCTTCCACCCTCCTGCCCCGTATACTATGGTGCCATTGGGAGGACTC
CCAGGCCACCAGGCCAGTGGACAGCCCTACCTCAGTGGCATCAGTGGACGGGCCTGTGCTAATGGGATCCACATG
AATAGGGGCTGCCCCCTCGGCTGCAGTGGGCTACCCGGGCATGAAGCCCCAGCAGCACTGCCCAGGCGAGCTTCAG
CAGCAGAGTGACACCAGCAGCCTGCTGAGGCAGACCCATCTTGGCAATGGATATGACCCCCAAAGTCACCAGATC
ACGAGGGGTCCCAAGTCTAGCCCGGACGAGGGCTCTTCTTATACACACTGCCCGACGACTCCACTCACCAGCTG
CTGCAGCCCCATCACGACTGCTGCCAACGCCAGGAGCAGCCTGCTGCTGTGGGCCAGTCAGGGGTGAGGAGAGCC
CCCGACAGTCTGTCTTGGAAAGCAGTGTGGGACCCCTCCATTTCACTCAGGGCCCCCATGCTGCTTGGGCCTTGTG
CCAGTTGAAGAGGTGGACAGTCTTGAAGTCTGCAAGTGAAGTGGAGGAGACTGGTGTCCCCAGCACCCCGTAGGG
GCCTACGTAGGACAGGAACCTGGAATGCAGCTCTCCCCGGGGCCACTGGTGGTGTGTCTTTTGAACACCACCT
CTCACAATTTAGGCAGAAGCTGATATCCCAGAAAGACTATATATTGTTTTTTTTTAAAAAAAAGAAGAAAA
AGAGACAGAGAAAATTGGTATTTATTTTCTATTATAGCCATATTTATATATTTATGCACTTGTAATAAATGTA
TATGTTTTATAATTCTGGAGAGACATAAGGAGTCTACCCGTTGAGGTTGGAGAGGGAAAATAAAGAAGCTGCCA
CCTAACAGGAGTCACCCAGGAAGCACCAGCAGGCTGGCGCGGGACAGACTCCTAACCTGGGGCCTCTGCAGTG
GCAGGCGAGGCTGCAGGAGGCCACAGATAAGCTGGCAAGAGGAAGGATCCCAGGCACATGGTTTCATCAGAGCA
TGAGGGAACAGCAAGGGGCACGGTATCACAGCCTGGAGACACCCACACAGATGGCTGGATCCGGTGTACGGGAA
ACATTTTCTAAGATGCCCATGAGAACAGACCAAGATGTGTACAGCACTATGAGCATTAATAAACCTTCCAGAAT
CAATAATCCGTGGCAACATATCTCTGTAAAAACAAACACTGTAACCTTAAATAAATGTTTAGTCTTCCCTGTAAAA

FIGURE 36

MLRGTM TAWRGMRPEVTLACLLLATAGCFADLNEVPQVTVQPASTVQKPGGT VILGCVVEPP
RMNV TWRLNGKELNGSDDALGVLITHGTLVITALNNHTVGRYQCVARMPAGAVASVPATVTL
ANLQDFKLDVQH VIEVDEGNTAVIACHLPESH PKAQVRYSVKQEWLEASRGNYLIMPSGNLQ
IVNASQEDEGMYKCAAYNPVTQE VKTSGSSDRLRVRRSTAEAAARI IYPPEAQTIIVTKGQSL
ILECVASGIPPPRV TWAKDGSSVTGYNKTRFLLSNLLIDTTSEEDSGTYRCMADNGVGQPGA
AVILYNVQVFEPPEVTMELS QLVI PWGQSAKLTCEVRGNPPPSVLWLRNAVPLISSQRLRLS
RRALRVLSMGPEDEGVYQCMAENEVGS AHAVVQLRTSRPSITPRLWQDAELATGTPPVSPSK
LGNPEQMLRGQPALPRPPTSVGPASPKCPGEGKGQGAPEAPIILSSPRTSKTDSYELVWRPR
HEGSGRAPILYYVVKHRKQVTNSSDDWTISGIPANQHRLTLTRLDPGSLYEVEMAAYNCAGE
GQTAMVTFRTGRRPKPEIMASKEQQIQRDDPGAS PQSSSQPDHGRLSPPEAPDRPTISTASE
TSVYVTWIPRGNGGFPIQSF RVEYKKLKKVGDWILATSAIPPSRLSVEITGLEKGTSYKFRV
RALNMLGESEPSAPSRPYV VSGYSGRVYERP VAGPYITFTDAVNETTIMLKWMI PASNNNT
PIHGFYIYYRPTDSDNDS DYKKDMVEGD KYWHSISHLQ PETS YDIKMQCFNEGGESEFSNVM
ICETKARKSSGQPGR LPPPTLAPPQPPLPETIERPVGTGAMVARSSDLPYLIVGVVLGSI VL
IIVTFIPFCLWRAW SKQKHTTDLGFPR SALPPSCPYTMVPLGGLPGHQASGQPYLSGISGRA
CANGIHMNRGCPSAAVGYPGMKPQQHCPGELQQQSDTSSLLRQTHLGNGYDPQSHQITRGPK
SSPDEGSFLYTL PDDSTHQLLQPHHDCCQRQE QPAAVGQSGVRRAPDSPVLEAVWDPPFHSG
PPCCLGLVPVEEVDSPDSCQVSGGDWCPQH PVGAYVGQEPGMQLSPGPLVRVSFETPPLTI

Signal peptide:

amino acids 1-30

Transmembrane domain:

amino acids 16-30 (type II), 854-879

FIGURE 37

CGGGAGGCTGGGTCGTCATGATCCGGACCCCATTTGTCGGCCTCTGCCCATCGCCTGCTCCTC
CCAGGCTCCCGCGGCCGACCCCGCGCAACATGCAGCCCACGGGCGCGAGGGTTCCCGCGC
GCTCAGCCGGCGGTATCTGCGGCGTCTGCTGCTCCTGCTACTGCTGCTGCTGCTGCGGCAGC
CCGTAACCCGCGCGGAGACCACGCCGGGCGCCCCCAGAGCCCTCTCCACGCTGGGCTCCCC
AGCCTCTTCACCACGCCGGGTGTCCCCAGCGCCCTCACTACCCAGGCCTCACTACGCCAGG
CACCCCCAAAACCTTGGACCTTCGGGGTTCGCGCGCAGGCCCTGATGCGGAGTTTCCCACTCG
TGGACGGCCACAATGACCTGCCCCAGGTCTTGAGACAGCGTTACAAGAATGTGCTTCAGGAT
GTTAACCTGCGAAATTTTCAGCCATGGTCAGACCAGCCTGGACAGGCTTAGAGACGGCCTCGT
GGGTGCCCAGTTCTGGTCAGCCTCCGTCTCATGCCAGTCCCAGGACCAGACTGCCGTGCGCC
TCGCCCTGGAGCAGATTGACCTCATTACCGCATGTGTGCCTCCTACTCTGAACCTCGAGCTT
GTGACCTCAGCTGAAGGTCTGAACAGCTCTCAAAGCTGGCCTGCCTCATTTGGCGTGNAGGG
TGGTCACTCACTGGACAGCAGCCTCTCTGTGCTGCGCAGTTTCTATGTGCTGGGGGTGCGCT
ACCTGACACTTACCTTCACCTGCAGTACACCATGGGCAGAGAGTTCCACCAAGTTCAGACAC
CACATGTACACCAACGTCAGCGGATTGACAAGCTTTGGTGAGAAAGTAGTAGAGGAGTTGAA
CCGCCTGGGCATGATGATAGATTTGTCTTATGCATCGGACACCTTGATAAGAAGGGTCCTGG
AAGTGTCTCAGGCTCCTGTGATCTTCTCCCACTCAGCTGCCAGAGCTGTGTGTGACAATTTG
TTGAATGTTCCCGATGATATCCTGCAGCTTCTGAAGAACGGTGGCATCGTGATGGTGACACT
GTCCATGGGGGTGCTGCAGTGCAACCTGCTTGCTAACGTGTCCACTGTGGCAGATCACTTTG
ACCACATCAGGGCAGTCATTGGATCTGAGTTCATCGGGATTGGTGGAATTTATGACGGGACT
GGCCGGTTCCCTCAGGGGCTGGAGGATGTGTCCACATACCCAGTCCTGATAGAGGAGTTGCT
GAGTCGTASCTGGAGCGAGGAAGAGCTTCAAGGTGTCCTTCGTGGAAACCTGCTGCGGGTCT
TCAGACAAGTGGAAAAGGTGAGAGAGGAGAGCAGGGCGCAGAGCCCCGTGGAGGCTGAGTTT
CCATATGGGCAACTGAGCACATCCTGCCACTCCCACCTCGTGCCTCAGAATGGACACCAGGC
TACTCATCTGGAGGTGACCAAGCAGCCAACCAATCGGGTCCCCTGGAGGTCCTCAAATGCCT
CCCCATACCTTGTTCCAGGCCTTGTGGCTGCTGCCACCATCCCAACCTTCACCCAGTGGCTC
TGCTGACCACAGTCGGTCCCCGCAGAGGTCACTGTGGCAAAGCCTCACAAGCCCCCTCTCCT
AGTTCATTCAAGCATATGCTGAGAATAAACATGTTACACATGGAAAA

FIGURE 38

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA59817

><subunit 1 of 1, 487 aa, 1 stop, 2 unknown

><MW: 53569.32, pI: 7.68, NX(S/T): 5

MQPTGREGSRALSRRYLRRLLLLLLLLLLLLLRQPVTRAETTPGAPRALSTLGSPSLFTTPGVPS
ALTTPGLTTPGTPKTLDLRGRAQALMRSFPLVDGHNDLPQVLRQRYKNVLQDVNLRNFSHGQ
TSLDRLRDGLVGAQFWSASVSCQSQDQTAVRLALEQIDLIHRMCASYSELELV TSAEGLNSS
QKLACLIGVXGGHSLDSSLSVLRSFYVLGVRYLTLTFTCSTPWAESSTKFRHHMYTNVSGLT
SFGEKVVEELNRLGMMIDLSYASDTLIRRVLEVSQAPVIFSHSAARAVCDNLLNVPDDILQL
LKNGGIVMVTLSMGVLQCNLLANVSTVADHFDHIRAVIGSEFIGIGGNYDGTGRFPQGLEDV
STYPVLIEELLSRXWSEEEELQGVLRGNLLRVFRQVEKVVREESRAQSPVEAEFPYGQLSTSCH
SHLVPQNGHQATHLEVTKQPTNRVPWRSSNASPYLVPGLVAAATIPTFTQWLC

Important features of the protein:

Signal peptide:

amino acids 1-36

Transmembrane domain:

amino acids 313-331

N-glycosylation sites.

amino acids 119-122, 184-187, 243-246 and 333-336

N-myristoylation sites.

amino acids 41-46, 59-64, 73-78, 133-138, 182-187, 194-199, 324-329, 354-359, 357-362, 394-399, 427-432 and 472-477.

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 136-146

FIGURE 39

TGCTAGGCTCTGTCCCACAATGCACCCGAGAGCAGGAGCTGAAAGCCTCTAACACCCACAGA
TCCCTCTATGACTGCAATGTGAGGTGTCCGGCTTTGCTGGCCCAGCAAGCCTGATAAGCATG
AAGCTCTTATCTTTGGTGGCTGTGGTCCGGTGTGTTGCTGGTGCCCCCAGCTGAAGCCAACAA
GAGTTCTGAAGATATCCGGTGCAAATGCATCTGTCCACCTTATAGAAACATCAGTGGGCACA
TTTACAACCAGAATGTATCCCAGAAGGACTGCAACTGCCTGCACGTGGTGGAGCCCATGCCA
GTGCCTGGCCATGACGTGGAGGCCTACTGCCTGCTGTGCGAGTGCAGGTACGAGGAGCGCAG
CACCACCACCATCAAGGTCATCATTGTCATCTACCTGTCCGTGGTGGGTGCCCTGTTGCTCT
ACATGGCCTTCCTGATGCTGGTGGACCCTCTGATCCGAAAGCCGGATGCATACACTGAGCAA
CTGCACAATGAGGAGGAGAATGAGGATGCTCGCTCTATGGCAGCAGCTGCTGCATCCCTCGG
GGGACCCCGAGCAAACACAGTCCTGGAGCGTGTGGAAGGTGCCCAGCAGCGGTGGAAGCTGC
AGGTGCAGGAGCAGCGGAAGACAGTCTTCGATCGGCACAAGATGCTCAGCTAGATGGGCTGG
TGTGGTTGGGTCAAGGCCCAACACCATGGCTGCCAGCTTCCAGGCTGGACAAAGCAGGGGG
CTACTTCTCCCTTCCTCGGTTCCAGTCTTCCCTTTAAAAGCCTGTGGCATTTCCTCCTT
CTCCCTAACTTTAGAAATGTTGTACTTGGCTATTTTGATTAGGGAAGAGGGATGTGGTCTCT
GATCTCTGTTGTCTTCTTGGGTCTTTGGGGTTGAAGGGAGGGGGAAGGCAGGCCAGAAGGGA
ATGGAGACATTGAGGCGGCCTCAGGAGTGGATGCGATCTGTCTCTCCTGGCTCCACTCTTG
CCGCCTTCAGCTCTGAGTCTTGGGAATGTTGTTACCCTTGGAAGATAAAGCTGGGTCTTCA
GGAACTCAGTGTCTGGGAGGAAAGCATGGCCCAGCATTGAGCATGTGTTTCCTTTCTGCAGTG
GTTCTTATCACCACCTCCCTCCCAGCCCCGGCGCCTCAGCCCCAGCCCCAGCTCCAGCCCTG
AGGACAGCTCTGATGGGAGAGCTGGGCCCCCTGAGCCCACTGGGTCTTCAGGGTGCACTGGA
AGCTGGTGTTGCTGTCCCCTGTGCACTTCTCGCACTGGGGCATGGAGTGCCCATGCATACT
CTGCTGCCGGTCCCCTCACCTGCACTTGAGGGGTCTGGGCAGTCCCTCCTCTCCCCAGTGTC
CACAGTCACTGAGCCAGACGGTCGGTTGGAACATGAGACTCGAGGCTGAGCGTGGATCTGAA
CACCACAGCCCCTGTACTTGGGTGCTCTGTCCTGAACTTCGTTGTACCAGTGCATGGA
GAGAAAATTTTGTCTCTTGTCTTAGAGTTGTGTGTAAATCAAGGAAGCCATCATTAATTG
TTTTATTTCTCTCA

FIGURE 40

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA60278

<subunit 1 of 1, 183 aa, 1 stop

<MW: 20574, pI: 6.60, NX(S/T): 3

MKLLSLVAVVGCLLVPPAEANKSSEDIRCKCICPPYRNISGHIYNQNVSQKDCNCLHVVEPM
PVPGHDVEAYCLLCECRYEERSTTTIKVIIIVYLSVVGALLLYMAFLMLVDPLIRKPDAYTE
QLHNEEENEDARSMAAAAASLGGPRANTVLERVEGAQQRWKLQVQEQRKTVFDRHKMLS

Important features:

Signal peptide:

amino acids 1-20

Transmembrane domain:

amino acids 90-112

N-glycosylation sites.

amino acids 21-24, 38-41 and 47-50

FIGURE 41

AGCGGGTCTCGCTTGGGTTCGCTAATTTCTGTCCTGAGGCGTGAGACTGAGTTCATAGGGTCCTGGGTCCCCGA
ACCAGGAAGGGTTGAGGGAACACAATCTGCAAGCCCCCGCGACCCAAGTGAGGGGCCCCGTGTTGGGGTCTCTCC
TCCCTTTGCATTCCCACCCCTCCGGGCTTTGCGTCTTCTGGGGACCCCTCGCCGGGAGATGGCCGCGTTGATG
CGGAGCAAGGATTCGTCTCTGCTGCTGCTCTACTGGCCGCGGTGCTGATGGTGGAGAGCTCACAGATCGGCAGT
TCGCGGGCCAACTCAACTCCATCAAGTCCTCTCTGGGCGGGGAGACGCCTGGTCAGGCCGCCAATCGATCTGCG
GGCATGTACCAAGGACTGGCATTCTGGCGGCAGTAAGAAGGGCAAAAACCTGGGGCAGGCCTACCCTTGTAGCAGT
GATAAGGAGTGTGAAGTTGGGAGGTATTGCCACAGTCCCCACCAAGGATCATCGGCCTGCATGGTGTGTCTGGAGA
AAAAAGAAGCGCTGCCACCGAGATGGCATGTGCTGCCCCAGTACCCGCTGCAATAATGGCATCTGTATCCCAGTT
ACTGAAAGCATCTTAACCCCTCACATCCCGGCTCTGGATGGTACTCGGCACAGAGATCGAAACCACGGTCATTAC
TCAAACCATGACTTGGGATGGCAGAATCTAGGAAGACCACACACTAAGATGTCACATATAAAAGGGCATGAAGGA
GACCCCTGCCTACGATCATCAGACTGCATTGAAGGGTTTTGCTGTGCTCGTCATTTCTGGACCAAATCTGCAAA
CCAGTGCTCCATCAGGGGGAAGTCTGTACCAAACAACGCAAGAAGGGTTCTCATGGGCTGGAAATTTTCCAGCGT
TGCGACTGTGCGAAGGGCCTGTCTTGCAAAGTATGGAAAGATGCCACCTACTCCTCCAAAGCCAGACTCCATGTG
TGTCAGAAAATTTGATCACCATTGAGGAACATCATCAATTGCAGACTGTGAAGTTGTGTATTTAATGCATTATAG
CATGGTGGAAAATAAGGTTTCAGATGCAGAAGAATGGCTAAAATAAGAAACGTGATAAGAATATAGATGATCACA
AAAGGGAGAAAGAAAACATGAAGTGAATAGATTAGAATGGGTGACAAATGCAGTGCAGCCAGTGTTCATTATG
CAACTTGTCTATGTAAATAATGTACACATTTGTGGAAAATGCTATTATTAAGAGAACAAGCACACAGTGGAAATT
ACTGATGAGTAGCATGTGACTTTTCCAAGAGTTTAGGTTGTGCTGGAGGAGAGGTTTCTTTCAGATTGCTGATTGC
TTATACAAATAACCTACATGCCAGATTTCTATTCAACGTTAGAGTTTAAACAAAATACTCCTAGAATAACTTGTTA
TACAATAGGTTCTAAAATAAAATTGCTAAACAAGAAATGAAAACATGGAGCATTGTTAATTTACAACAGAAAAT
TACCTTTTGATTTGTAACACTACTTCTGCTGTTCAATCAAGAGTCTTGGTAGATAAGAAAAAAATCAGTCAATAT
TTCCAAATAATTGCAAAATAATGGCCAGTTGTTTAGGAAGGCCCTTTAGGAAGACAAATAAATAACAAACAAACAG
CCACAAATACTTTTTTTTCAAAATTTTAGTTTTACCTGTAATTAATAAGAACTGATACAAGACAAAAACAGTTCC
TTCAGATTCTACGGAATGACAGTATATCTCTCTTATCCTATGTGATTCTGCTCTGAATGCATTATATTTTCCA
AACTATACCCATAAATTGTGACTAGTAAATACTTACACAGAGCAGAATTTTCACAGATGGCAAAAAAATTTAA
GATGTCCAATATATGTGGGAAAAGAGCTAACAGAGAGATCATTATTTCTTAAAGATTGGCCATAACCTATATTTT
GATAGAATTAGATTGGTAAATACATGTATTCATACATACTCTGTGGTAATAGAGACTTAAGCTGGATCTGTACTG
CACTGGAGTAAGCAAGAAAATTTGGGAAAACTTTTTCGTTTGTTCAGGTTTTGGCAACACATAGATCATATGCTCTG
AGGCACAAGTTGGCTGTTTCATCTTTGAAACCAGGGGATGCACAGTCTAAATGAATATCTGCATGGGATTTGCTAT
CATAATATTTACTATGCAGATGAATTCAGTGTGAGGTCCTGTGTCCGTACTATCCTCAAATTATTTATTTTATAG
TGCTGAGATCCTCAAATAATCTCAATTTTCAAGAGGTTTCACAAAATGTACTCCTGAAGTAGACAGAGTAGTGAGG
TTTCATTGCCCTCTATAAGCTTCTGACTAGCCAATGGCATCATCCAATTTTCTTCCCAAACCTCTGCAGCATCTG
CTTTATTGCCAAAGGGCTAGTTTCGGTTTTCTGCAGCCATTGCGGTTAAAAAATATAAGTAGGATAACTTGTA
ACCTGCATATTGCTAATCTATAGACACCACAGTTTCTAAATTCCTTGAAACCCTTTACTACTTTTTTTAACTT
AACTCAGTTCTAAATACTTTGTCTGGAGCACAAAACAATAAAAGGTTATCTTATAGTCGTGACTTTAACTTTTG
TAGACCACAATTCACTTTTTAGTTTTCTTTTACTTAAATCCCATCTGCAGTCTCAAATTTAAGTTCTCCAGTAG
AGATTGAGTTTGAGCCTGTATATCTATTAATAAATTTCAACTTCCCACATATATTTACTAAGATGATTAAGACTTA
CATTTTCTGCACAGGTCTGCAAAAACAAAATTATAAACTAGTCCATCCAAGAACCAAAGTTTGTATAAACAGGT
TGCTATAAGCTTGTGAAATGAAAATGGAACATTTCAATCAAACATTTCCCTATATAACAATTATTATATTTACAAT
TTGGTTTCTGCAATATTTTTCTTATGTCCACCCTTTTAAAAATTATTATTTGAAGTAATTTATTACAGGAAATG
TTAATGAGATGTATTTTCTTATAGAGATATTTCTTACAGAAAGCTTTGTAGCAGAATATATTTGCAGCTATTGAC
TTTGTAATTTAGGAAAAATGTATAATAAGATAAAATCTATTAAATTTTCTCCTCTAAAAACTGAAAAA
AAAAAAAAAAAAAAAAAAAA

FIGURE 42

MAALMRSKDSSCCLLLLLAAVLMVESSQIGSSRAKLNSIKSSLGGETPGQAANRSAGMYQGLA
FGGSKKGKNLGQAYPCSSDKECEVGRYCHSPHQGSSACMVCRRKKRCHRDGMCCPSTRCNN
GICIPVTESILTPHIPALDGTRHRDRNHGHYSNHDLGWQNLGRPHTKMSHIKGHEGDPCLRS
SDCIEGFCCARHFWTKICKPVLHQGEVCTKQRKKGSHGLEIFQRCDCAKGLSCKVWKDATYS
SKARLHVCQKI

Signal peptide:

amino acids 1-25

FIGURE 43

TCTCAATCTGCTGACCTCGTGATCCGCCTGACCTTGTAATCCACCTACCTTGGCCTCCCAA
GTGTTGGGATTACAGGCGTGAGCCACCGCGCCCGGCCAACATCACGTTTTTAAAAATTGATT
TCTTCAAATTCATGGCAAATATTTCCCTTCCCTTTAACTTCTTATGTCAGAATGAGGAAGGA
TAGCTGCATTTATTTAGTCAGTTTTTCATTGCATAGTAATATTTTCATGTAGTATTTTCTAAG
TTATATTTTAGTAATTCATATGTTTTAGATTATAGGTTTTAACATACTTGTGAAAATACTTG
ATGTGTTTTAAAGCCTTGGGCAGAAATTCTGTATTGTTGAGGATTTGTTCTTTTATCCCCCT
TTTAAAGTCATCCGTCCTTGGCTCAGGATTTGGAGAGCTTGCACCACCAAAAATGGCAAACA
TCACCAGCTCCCAGATTTTGGACCAGTTGAAAGCTCCGAGTTTGGGCCAGTTTACCACCACC
CCAAGTACACAGCAGAATAGTACAAGTCACCCTACAACCTACTACTTCTTGGGACCTCAAGCC
CCCAACATCCCAGTCCTCAGTCCTCAGTCATCTTGACTTCAAATCTCAACCTGAGCCATCCC
CAGTTCTTAGCCAGTTGAGCCAGCGACAACAGCACCAGAGCCAGGCAGTCACTGTTCTCTCT
CCTGGTTTGGAGTCCTTTCCTTCCCAGGCAAACTTCGAGAATCAACACCTGGAGACAGTCC
CTCCACTGTGAACAAGCTTTTGCAGCTTCCCAGCAGCACCATTGAAAATATCTCTGTGTCTG
TCCACCAGCCACAGCCCAAACACATCAAACCTTGCTAAGCGGCGGATACCCCCAGCTTCTAAG
ATCCCAGCTTCTGCAGTGGAAATGCCTGGTTCAGCAGATGTCACAGGATTAAATGTGCAGTT
TGGGGCTCTGGAATTTGGGTCAGAACCTTCTCTCTCTGAATTTGGATCAGCTCCAAGCAGTG
AAAATAGTAATCAGATTCCCATCAGCTTGTATTCGAAGTCTTTAAGTGAGCCTTTGAATACA
TCTTTATCAATGACCAGTGCAGTACAGAACTCCACATATACAACTTCCGTCATTACCTCCTG
CAGTCTGACAAGCTCATCACTGAATTCTGCTAGTCCAGTAGCAATGTCTTCCTCTTATGACC
AGAGTTCTGTGCATAACAGGATCCCATACCAAAGCCCTGTGAGTTCATCAGAGTCAGCTCCA
GGAACCATCATGAATGGACATGGTGGTGGTGAAGTCAGCAGACACTAGACAGTAAGTATAG
CAGCAAGCTACTCTTGTCATGGCTGGTGCCAACCAAACAGAGGAAGAGGATAGCTCACGTGA
TGTGGAAAACACCAGTTGGTCAATGGCTCATTCGTTAAAAAGCAGCCCTTTTGCTTTTTTGT
TTTTGGACCAGGTGTTGGCTGTGGTGTATTAGAAATGTCTTAACCACAGCAAGAAGGAGGT
GGTGGTCTCATATTCTTCTGCCCTAATCAGACTGCACCACAAGTGCAGCATAACAGTATGCAT
TTTAAAGATGCTTGGGCCAGGCGGGGTGGCTGATGCCCATAAATCCCAGTGCTTTGGGGGGCC
AAGGCAGGCAGATTGCCCAAGCTCAGGAGTTTGAGACCACCCTGGGCAACATGGTGAAACTC
TGTCTCTACTAAAATACGAAAACTAGCCGGGTGTGGTGGCGGCGCGTGCCTGTAATCCCAG
CTACTTGGGAGGCTGAGGCACAAGAATCGCTTGAGCCAGCTTGGGCTACAAAGTGAGACTCC
GTCTGAAAAGA

FIGURE 44

MCFKALGRNSVLLRICSFIPLLKSSVLGSGFGELAPPKMANITSSQILDQLKAPSLGQFTTT
PSTQQNSTSHPTTTTTSWDLKPPTSQSSVLSHLDFKSQPEPSPVLSQLSQRQQHQSQAVTVPP
PGLESFPSQAKLRESTPGDSPSTVNKLLQLPSTTIENISVSVHQPPQPKHIKLAKRRIPPASK
IPASAVEMPGSADVTGLNVQFGALEFGSEPSLSEFGSAPSSSENSNQIPISLYSKSLSEPLNT
SLSMTSAVQNSTYTTTSVITSCSLTSSSLNSASPVAMSSSYDQSSVHNRIPTYQSPVSSSESAP
GTIMNGHGGGRSQQTLDISKYSSKLLLSWLVP TKQRKRIAHVMWKTPVGQWLIR

Signal peptide:

amino acids 1-24

FIGURE 45

GCCGAGTGGGACAAAGCCTGGGGCTGGGCGGGGGGCCATGGCGCTGCCATCCCGAATCCTGCT
TTGGAAACTTGTGCTTCTGCAGAGCTCTGCTGTTCTCCTGCACTCAGCGGTGGAGGAGACGG
ACGCGGGGCTGTACACCTGCAACCTGCACCATCACTACTGCCACCTCTACGAGAGCCTGGCC
GTCCGCCTGGAGGTCACCGACGGCCCCCGGCCACCCCGCCTACTGGGACGGCGAGAAGGA
GGTGCTGGCGGTGGCGCGCGGCGCACCCGCGCTTCTGACCTGCGTGAACCGCGGGCACGTGT
GGACCGACCGGCACGTGGAGGAGGCTCAACAGGTGGTGCCTGGGACCGGCAGCCGCCCGGG
GTCCCGCACGACCGCGCGGACCGCCTGCTGGACCTCTACGCGTCGGGCGAGCGCCGCGCCTA
CGGGCCCCCTTTTTCTGCGCGACCGCGTGGCTGTGGGCGCGGATGCCTTTGAGCGCGGTGACT
TCTCACTGCGTATCGAGCCGCTGGAGGTGCGCGACGAGGGCACCTACTCCTGCCACCTGCAC
CACCATTACTGTGGCCTGCACGAACGCCGCGTCTTCCACCTGACGGTCGCCGAACCCACGC
GGAGCCGCCCCCGGGGCTCTCCGGGCAACGGCTCCAGCCACAGCGGCGCCCCAGGCCCCAG
ACCCACACTGGCGCGCGGCCACAACGTCATCAATGTCATCGTCCCCGAGAGCCGAGCCCAC
TTCTTCCAGCAGCTGGGCTACGTGCTGGCCACGCTGCTGCTCTTCATCCTGCTACTGGTCAC
TGTCCTCCTGGCCGCCCCGAGGCGCCGCGGAGGCTACGAATACTCGGACCAGAAGTCGGGAA
AGTCAAAGGGGAAGGATGTTAACTTGGCGGAGTTCGCTGTGGCTGCAGGGGACCAGATGCTT
TACAGGAGTGAGGACATCCAGCTAGATTACAAAAACAACATCCTGAAGGAGAGGGCGGAGCT
GGCCACAGCCCCCTGCCTGCCAAGTACATCGACCTAGACAAAGGGTTCCGGAAGGAGAACT
GCAAATAGGGAGGCCCTGGGCTCCTGGCTGGGCCAGCAGCTGCACCTCTCCTGTCTGTGCTC
CTCGGGGCATCTCCTGATGCTCCGGGGCTCACCCCCCTTCCAGCGGCTGGTCCCGCTTTCT
GGAATTTGGCCTGGGCGTATGCAGAGGCCGCTCCACACCCCTCCCCAGGGGCTTGGTGGC
AGCATAGCCCCCACCCCTGCGGCCTTTGCTCACGGGTGGCCCTGCCACCCCTGGCACAACC
AAAATCCCCTGATGCCCATCATGCCCTCAGACCCCTTCTGGGCTCTGCCCGCTGGGGGCTG
AAGACATTCTGGAGGACACTCCCATCAGAACCTGGCAGCCCCAAAAGTGGGGTCAGCCTCA
GGGCAGGAGTCCCACTCCTCCAGGGCTCTGCTCGTCCGGGGCTGGGAGATGTTCTGGAGGA
GGACACTCCCATCAGAACTTGGCAGCCTTGAAGTTGGGGTCAGCCTCGGCAGGAGTCCCACT
CCTCCTGGGGTGCTGCCTGCCACCAAGAGCTCCCCACCTGTACCACCATGTGGGACTCCAG
GCACCATCTGTTCTCCCCAGGGACCTGCTGACTTGAATGCCAGCCCTTGCTCCTCTGTGTTG
CTTTGGGCCACCTGGGGCTGCACCCCTGCCCTTTCTCTGCCCCATCCCTACCCTAGCCTTG
CTCTCAGCCACCTTGATAGTCACTGGGCTCCCTGTGACTTCTGACCCCTGACACCCCTCCCTT
GGACTCTGCCTGGGCTGGAGTCTAGGGCTGGGGCTACATTTGGCTTCTGTACTGGCTGAGGA
CAGGGGAGGGAGTGAAGTTGGTTTGGGGTGGCCTGTGTTGCCACTCTCAGCACCCACATTT
GCATCTGCTGGTGGACCTGCCACCATCACAATAAAGTCCCCATCTGATTTTTTAAAAA
AAAAA

FIGURE 46

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA60618

<subunit 1 of 1, 341 aa, 1 stop

<MW: 38070, pI: 6.88, NX(S/T): 1

MALPSRILLWKLVLQSSAVLLHSAVEETDAGLYTCNLHHHYCHLYESLAVRLEVTDGPPAT
PAYWDGEKEVLAVARGAPALLTCVNRGHVWTD RHVEEAQQVVHWRQPPGVPHDRADRLDL
YASGERRAYGPLFLRDRVAVGADAFERGFSLRIEPLVADEGTYSCHLHHHYCGLHERRVF
HLTVAEPHAEPFPRGSPGNGSSHSGAPGPDPTLARGHNVINVIVPESRAHFFQQLGYVLATL
LLFILLLVTVLLAARRRRGGYEYSDQKSGKSKGKDVNLAFAVAAGDQMLYRSEDIQLDYKN
NILKERAELAHSPLPAKYIDLDKGFRKENCK

Important features:

Signal peptide:

amino acids 1-19

Transmembrane domain:

amino acids 237-262

N-glycosylation site.

amino acids 205-208

Cell attachment sequence.

amino acids 151-154

Coproporphyrinogen III oxidase proteins.

amino acids 115-140

FIGURE 47

CGCCGGAGGCAGCGGCGGCGTGGCGCAGCGGCGACATGGCCGTTGTCTCAGAGGACGACTTT
CAGCACAGTTCAAACCTCCACCTACGGAACCACAAGCAGCAGTCTCCGAGCTGACCAGGAGGC
ACTGCTTGAGAAGCTGCTGGACCGCCCGCCCCCTGGCCTGCAGAGGCCCGAGGACCGCTTCT
GTGGCACATACATCATCTTCTTCAGCCTGGGCATTGGCAGTCTACTGCCATGGAACTTCTTT
ATCACTGCCAAGGAGTACTGGATGTTCAAACCTCCGCAACTCCTCCAGCCCAGCCACCGGGGA
GGACCCTGAGGGCTCAGACATCCTGAACTACTTTGAGAGCTACCTTGCCGTTGCCTCCACCG
TGCCCTCCATGCTGTGCCTGGTGGCCAACTTCCTGCTTGTCAACAGGGTTGCAGTCCACATC
CGTGTCCTGGCCTCACTGACGGTCATCCTGGCCATCTTCATGGTGATAACTGCACTGGTGAA
GGTGGACACTTCCTCCTGGACCCGTGGTTTTTTTTGCGGTCAACATTGTCTGCATGGTGATCC
TCAGCGGTGCCTCCACTGTCTTCAGCAGCAGCATCTACGGCATGACCGGCTCCTTTCCTATG
AGGAACTCCCAAGCACTGATATCAGGAGGAGCCATGGGCGGGACGGTCAGCGCCGTGGCCTC
ATTGGTGGACTTGGCTGCATCCAGTGATGTGAGGAACAGCGCCCTGGCCTTCTTCCTGACGG
CCACCATCTTCCTCGTGCTCTGCATGGGACTCTACCTGCTGCTGTCCAGGCTGGAGTATGCC
AGGTACTACATGAGGCCTGTTCTTGCGGCCCATGTGTTTTCTGGTGAAGAGGAGCTTCCCCA
GGACTCCCTCAGTGCCCCCTTCGGTGGCCTCCAGATTCAATTGATTCCCACACACCCCCCTCTCC
GCCCCATCCTGAAGAAGACGGCCAGCCTGGGCTTCTGTGTACCTACGTCTTCTTCATCACC
AGCCTCATCTACCCCGCCGTCTGCACCAACATCGAGTCCCTCAACAAGGGCTCGGGCTCACT
GTGGACCACCAAGTTTTTCATCCCCCTCACTACCTTCCTCCTGTACAACCTTTGCTGACCTAT
GTGGCCCGGCAGCTCACCGCCTGGATCCAGGTGCCAGGGCCCAACAGCAAGGCGCTCCCAGGG
TTCGTGCTCCTCCGGACCTGCCTCATCCCCCTCTTCGTGCTCTGTAACTACCAGCCCCGCGT
CCACCTGAAGACTGTGGTCTTCCAGTCCGATGTGTACCCCGCACTCCTCAGCTCCCTGCTGG
GGCTCAGCAACGGCTACCTCAGCACCTGGCCCTCCTCTACGGGGCCTAAGATTGTGCCCAGG
GAGCTGGCTGAGGCCACGGGAGTGGTGATGTCCTTTTATGTGTGCTTGGGCTTAACACTGGG
CTCAGCCTGCTCTACCCTCCTGGTGCACCTCATCTAGAAAGGGAGGACACAAGGACATTGGTG
CTTCAGAGCCTTTGAAGATGAGAAGAGAGTGCAGGAGGGCTGGGGGCCATGGAGGAAAGGCC
TAAAGTTTCACTTGGGGACAGAGAGCAGAGCACACTCGGGCCTCATCCCTCCCAAGATGCCA
GTGAGCCACGTCCATGCCCATTCCGTGCAAGGCAGATATTCCAGTCATATTAACAGAACACT
CCTGAGACAGTTGAAGAAGAAATAGCACAAATCAGGGGTACTCCCTTCACAGCTGATGGTTA
ACATTCCACCTTCTTTCTAGCCCTTCAAAGATGCTGCCAGTGTTCCGCCCTAGAGTTATTACA
AAGCCAGTGCCAAAACCCAGCCATGGGCTCTTTGCAACCTCCCAGCTGCGCTCATTCCAGCT
GACAGCGAGATGCAAGCAAATGCTCAGCTCTCCTTACCCTGAAGGGGTCTCCCTGGAATGGA
AGTCCCCTGGCATGGTCAGTCCTCAGGCCCAAGACTCAAGTGTGCACAGACCCCTGTGTTCT
GCGGGTGAACAACTGCCCACTAACCAGACTGGAAAACCCAGAAAGATGGGCCTTCCATGAAT
GCTTCATTCCAGAGGGACCAGAGGGCCTCCCTGTGCAAGGGATCAAGCATGTCTGGCCTGGG
TTTTCAAAAAAAGAGGGATCCTCATGACCTGGTGGTCTATGGCCTGGGTCAAGATGAGGGTC
TTTCAGTGTTCTGTTTACAACATGTCAAAGCCATTGGTTCAAGGGCGTAATAAATACTTGC
GTATTCAAAAA

FIGURE 48

MAVSEDDFQHSSNSTYGTSSSLRADQEALLEKLLDRPPPGLQRPEDRFCGTYIIFFSLGI
GSLLPWNFFITAKEYWMFKLRNSSSPATGEDPEGSDILNYFESYLAVASTVPSMLCLVANFL
LVNRVAVHIRVLASLTVILAI FMVITALVKVDTSSWTRGFFAVTIVCMVILSGASTVFSSSI
YGMTGSFPMRNSQALISGGAMGGTVSAVASLVDLAASSDVRNSALAFFLTATIFLVLCMGLY
LLLSRLEYARYYMRPVLA AHVFSGEEELPQDSL SAPSVASRFIDSHTPPLRPILKKTASLGF
CVTYVFFITS LIYPAVCTNIESLNKGSGSLWTTKFFIPLTTFLLYNFADLCGRQLTAWIQVP
GPNSKALPGFVLLRTCLIPFLVLCNYQPRVHLKTVVFQSDVYPALLSSLLGLSNGYLSTLAL
LYGPKIVPRELAEATGVVMSFYVCLGLTLGSACSTLLVHLI

Transmembrane domain:

amino acids 50-74 (type II), 105-127, 135-153, 163-183, 228-252,
305-330, 448-472

FIGURE 49

GACAGTGGAGGGCAGTGGAGAGGACCGCGCTGTCCTGCTGTCACCAAGAGCTGGAGACACCA
TCTCCACCGAGAGTCAATGGCCCCATTGGCCCTGCACCTCCTCGTCCTCGTCCCCATCCTCC
TCAGCCTGGTGGCCTCCCAGGACTGGAAGGCTGAACGCAGCCAAGACCCCTTCGAGAAATGC
ATGCAGGATCCTGACTATGAGCAGCTGCTCAAGGTGGTGACCTGGGGGCTCAATCGGACCCT
GAAGCCCCAGAGGGTGATTGTGGTTGGCGCTGGTGTGGCCGGGCTGGTGGCCGCCAAGGTGC
TCAGCGATGCTGGACACAAGGTCACCATCCTGGAGGCAGATAACAGGATCGGGGGCCGCATC
TTCACCTACCGGGACCAGAACACGGGCTGGATTGGGGAGCTGGGAGCCATGCGCATGCCAG
CTCTCACAGGATCCTCCACAAGCTCTGCCAGGGCCTGGGGCTCAACCTGACCAAGTTCACCC
AGTACGACAAGAACACGTGGACGGAGGTGCACGAAGTGAAGCTGCGCAACTATGTGGTGGAG
AAGGTGCCCCGAGAAGCTGGGCTACGCCTTGCGTCCCCAGGAAAAGGGCCACTCGCCCCGAAGA
CATCTACCAGATGGCTCTCAACCAGGCCCTCAAAGACCTCAAGGCACTGGGCTGCAGAAAGG
CGATGAAGAAGTTTGAAAGGCACACGCTCTTGGAATATCTTCTCGGGGAGGGGAACCTGAGC
CGGCCGGCCGTGCAGCTTCTGGGAGACGTGATGTCCGAGGATGGCTTCTTCTATCTCAGCTT
CGCCGAGGCCCTCCGGGCCCACAGCTGCCTCAGCGACAGACTCCAGTACAGCCGCATCGTGG
GTGGCTGGGACCTGCTGCCGCGCGCGCTGCTGAGCTCGCTGTCCGGGCTTGTGCTGTTGAAC
GCGCCCGTGGTGGCGATGACCCAGGGACCGCACGATGTGCACGTGCAGATCGAGACCTCTCC
CCCGGCGCGGAATCTGAAGGTGCTGAAGGCCGACGTGGTGCTGCTGACGGCGAGCGGACCGG
CGGTGAAGCGCATCACCTTCTCGCCGCCGCTGCCCCGCCACATGCAGGAGGCGCTGCGGAGG
CTGCACTACGTGCCGGCCACCAAGGTGTTCTTAAGCTTCCGCAGGCCCTTCTGGCGCGAGGA
GCACATTGAAGGCGGCCACTCAAACACCGATCGCCCGTCGCGCATGATTTTCTACCCGCCGC
CGCGCGAGGGCGCGCTGCTGCTGGCCTCGTACACGTGGTTCGGACGCGGCGGCAGCGTTCCGC
GGCTTGAGCCGGGAAGAGGCGTTGCGCTTGGCGCTCGACGACGTGGCGGCATTGCACGGGCC
TGTCGTGCGCCAGCTCTGGGACGGCACCGGCGTCGTCAAGCGTTGGGCGGAGGACCAGCACA
GCCAGGGTGGCTTTGTGGTACAGCCGCCGGCGCTCTGGCAAACCGAAAAGGATGACTGGACG
GTCCCTTATGGCCGCATCTACTTTGCCGGCGAGCACACCGCCTACCCGCACGGCTGGGTGGA
GACGGCGGTCAAGTCGGCGCTGCGCGCCGCCATCAAGATCAACAGCCGGAAGGGGCCTGCAT
CGGACACGGCCAGCCCCGAGGGGCACGCATCTGACATGGAGGGGCAGGGGCATGTGCATGGG
GTGGCCAGCAGCCCCTCGCATGACCTGGCAAAGGAAGAAGGCAGCCACCCTCCAGTCCAAGG
CCAGTTATCTCTCCAAAACACGACCCACACGAGGACCTCGCATTAAAGTATTTTCGGAAAAA
AAA

FIGURE 50

MAPLALHLLVLPILLSLVASQDWKAERSQDPFEKCMQDPDYEQLLKVVWGLNRTLKPQRV
IVVGAGVAGLVAAKVLS DAGHKVTILEADNRIGGRIFTYRDQNTGWIGELGAMRMPSSHRIL
HKLCQGLGLNLTKFTQYDKNTWTEVHEVKLRNYVVEKVPEKLG YALRPQEKGHSPEDIYQMA
LNQALKDLKALGCRKAMKKFERHTLLEYLLGEGNLSRPAVQLLGDVMS EDGFFYLSFAEALR
AHSCLSDRLQYSRIVGGWDL LPRALLSSLSGLVLLNAPVVAMTQGP HDVHVQIETSPPARNL
KVLKADVLLTASGPAVKRITFSPPLPRHMQEALRRLHYVPATKVFLSFRRPFWREEHIEGG
HSNTDRPSRMIFYPPPREGALLLAS YTWSDAAAAFAGLSREEALRLALDDVAALHGPVVRQL
WDGTGVVKRWAEDQHSQGGFVVQPPALWQTEKDDWTVPYGRIYFAGEHTAYPHGWVETAVKS
ALRAAIKINSRKGPASDTASPEGHASDMEGQGHVHGVASSPSHDLAKEEGSHPPVQGQLSLQ
NTTHTRTSH

Signal peptide:

amino acids 1-21

FIGURE 51

CTGACATGGCCTGACTCGGGACAGCTCAGAGCAGGGCAGAACTGGGGACACTCTGGGCCGGCCTTCTG
CCTGCATGGACGCTCTGAAGCCACCCTGTCTCTGGAGGAACCACGAGCGAGGGAAGAAGGACAGGGAC
TCGTGTGGCAGGAAGAACTCAGAGCCGGGAAGCCCCCATTCACTAGAAGCACTGAGAGATGCGGCCCC
CTCGCAGGGTCTGAATTTCTGCTGCTGTTACAAAGATGCTTTTTATCTTTAACTTTTTGTTTTCCC
CACTTCCGACCCCGGCGTTGATCTGCATCCTGACATTTGGAGCTGCCATCTTCTTGTGGCTGATCACC
AGACCTCAACCCGTCTTACCTCTTCTTGACCTGAACAATCAGTCTGTGGGAATTGAGGGAGGAGCAGC
GAAGGGGGTTTCCCAGAAGAACAATGACCTAACAAGTTGCTGCTTCTCAGATGCCAAGACTATGTATG
AGGTTTTCCAAAGAGGACTCGCTGTGTCTGACAATGGGCCCTGCTTGGGATATAGAAAACCAAACCAG
CCCTACAGATGGCTATCTTACAAACAGGTGTCTGATAGAGCAGAGTACCTGGGTTCTGTCTCTTGCA
TAAAGGTTATAAATCATCACCAGACCAGTTTGTGCGCATCTTTGCTCAGAATAGGCCAGAGTGGATCA
TCTCCGAATTGGCTTGTTACACGTACTCTATGGTAGCTGTACCTCTGTATGACACCTTGGGACCAGAA
GCCATCGTACATATTGTCAACAAGGCTGATATCGCCATGGTGATCTGTGACACACCCCAAAGGCATT
GGTGCTGATAGGGAATGTAGAGAAAGGCTTCACCCCGAGCCTGAAGGTGATCATCCTTATGGACCCCT
TTGATGATGACCTGAAGCAAAGAGGGGAGAAGAGTGGAATTGAGATCTTATCCCTATATGATGCTGAG
AACCTAGGCAAAGAGCACTTCAGAAAACCTGTGCCTCCTAGCCCAGAAGACCTGAGCGTCATCTGCTT
CACCAGTGGGACCACAGGTGACCCCAAAGGAGCCATGATAACCCATCAAATATTGTTTCAAATGCTG
CTGCCTTTCTCAAATGTGTGGAGCATGCTTATGAGCCCACTCCTGATGATGTGGCCATATCCTACCTC
CCTCTGGCTCATATGTTTGAGAGGATTGTACAGGCTGTTGTGTACAGCTGTGGAGCCAGAGTTGGATT
CTTCCAAGGGGATATTCGGTTGCTGGCTGACGACATGAAGACTTTGAAGCCACATTGTTTCCCGCGG
TGCTTCGACTCCTTAACAGGATCTACGATAAGGTACAAAATGAGGCCAAGACACCCCTGAAGAAGTTC
TTGTTGAAGCTGGCTGTTTCCAGTAAATTCAAAGAGCTTCAAAGGGTATCATCAGGCATGATAGTTT
CTGGGACAAGCTCATCTTTGCAAAGATCCAGGACAGCCTGGGCGGAAGGGTTCGTGTAATTGTCACTG
GAGCTGCCCCCATGTCCACTTCAGTCATGACATTCTTCCGGGCAGCAATGGGATGTCAGGTGTATGAA
GCTTATGGTCAAACAGAATGCACAGGTGGCTGTACATTTACATTACCTGGGGACTGGACATCAGGTCA
CGTTGGGGTGCCCCCTGGCTTGCAATTACGTGAAGCTGGAAGATGTGGCTGACATGAACTACTTTACAG
TGAATAATGAAGGAGAGGTCTGCATCAAGGGTACAACCGTGTCAAAGGATACCTGAAGGACCCTGAG
AAGACACAGGAAGCCCTGGACAGTGATGGCTGGCTTACACAGGAGACATTGGTCTGCTGGCTCCCGAA
TGGAACCTCTGAAGATCATCGACCGTAAAAAGAACATTTTCAAGCTGGCCCAAGGAGAATACATTGCAC
CAGAGAAGATAGAAAATATCTACAACAGGAGTCAACCAGTGTTACAAATTTTTGTACACGGGGAGAGC
TTACGGTCATCCTTAGTAGGAGTGGTGGTTCCTGACACAGATGTACTTCCCTCATTTGCAGCCAAGCT
TGGGGTGAAGGGCTCCTTTGAGGAACTGTGCCAAAACCAAGTTGTAAGGGAAGCCATTTTAGAAGACT
TGCAGAAAATTGGGAAAGAAAGTGGCCTTAAACTTTTGAACAGGTCAAAGCCATTTTCTTCATCCA
GAGCCATTTTCCATTGAAAATGGGCTCTTGACACCAACATTGAAAGCAAAGCGAGGAGAGCTTTCCAA
ATACTTTTCGGACCCAAATTGACAGCCTGTATGAGCACATCCAGGATTAGGATAAGGTACTTAAGTACC
TGCCGGCCCCACTGTGCACTGCTTGTGAGAAAATGGATTAAAACTATTCTTACATTTGTTTTGCCTTT
CCTCCTATTTTTTTTTTAACCTGTAAACTCTAAAGCCATAGCTTTTGTGTTTTATATTGAGACATATAAT
GTGTAAACTTAGTTCCCAAATAAATCAATCCTGTCTTTCCCATCTTCGATGTTGCTAATATTAAGGCT
TCAGGGCTACTTTTATCAACATGCCTGTCTTCAAGATCCCAGTTTATGTTCTGTGTCCTTCCTCATGA
TTTCCAACCTTAATACTATTAGTAACCACAAGTTCAAGGGTCAAAGGGACCCTCTGTGCCTTCTTCTT
TGTTTTGTGATAAACATAACTTGCCAACAGTCTCTATGCTTATTTACATCTTCTACTGTTCAAACATAA
GAGATTTTTAAATTCTGAAAACTGCTTACAATTCATGTTTTCTAGCCACTCCACAAACCACTAAAT
TTTAGTTTTAGCCTATCACTCATGTCAATCATATCTATGAGACAAATGTCTCCGATGCTCTTCTGCGT
AAATTAAATTGTGTACTGAAGGGAAAAGTTTGATCATAACCAACATTTCTTAACTCTCTAGTTAGAT
ATCTGACTTGGGAGTATTAATAATTGGGTCTATGACATACTGTCCAAAAGGAATGCTGTTCTTAAAGC
ATTATTTACAGTAGGAAGTGGGGAGTAAATCTGTTCCCTACAGTTTGCTGCTGAGCTGGAAGCTGTGG
GGGAAGGAGTTGACAGGTGGGCCCAGTGAACCTTTTCCAGTAAATGAAGCAAGCACTGAATAAAAACCT
CCTGAACTGGGAACAAAGATCTACAGGCAAGCAAGATGCCACACAACAGGCTTATTTTCTGTGAAGG
AACCAACTGATCTCCCCACCCTTGATTAGAGTTCCTGCTCTACCTTACCCACAGATAACACATGTT
GTTTCTACTTGTAATGTAAAGTCTTTAAATAAACTATTACAGATAAAAAA

FIGURE 52

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA60775

<subunit 1 of 1, 739 aa, 1 stop

<MW: 82263, pI: 7.55, NX(S/T): 3

MDALKPPCLWRNHERGKKDRDSCGRKNSEPGSPHSLEALRDAAPSQGLNFLLLFTKMLFIFN
FLFSPLPTPALICILTFGAAIFLWLITRPQPVLPLLDLNNQSVGIEGGARKGVSQKNNDLTS
CCFSDAKTMYEVFQRGLAVSDNGPCLGYRKPNQPYRWLSYKQVSDRAEYLGSCLLHKGYKSS
PDQFVGIFAQNRPEWIISELACYTYSMAVAVPLYDTLGPEAIVHIVNKADIAMVICDTPQKAL
VLIGNVEKGFTPSLKVIILMDPFDDDLKQGEKSGIEILSLYDAENLGKEHFRKPVPPSPED
LSVICFTSGTTGDPKGAMITHQNIVSNAAFLKCV E HAYEPTPDDVAISYLPLAHMFERIVQ
AVVYSCGARVGFFQGDIRLLADDMKTLKPTLFPVPRLLNRIYDKVQNEAKTPLKKFLLKLA
VSSKFKELOKGIIRHDSFWDKLIFAKIQDSLGRVRVIVTGAAPMSTSVMTFFRAAMGCQVY
EAYGQTECTGGCTFTLPGDWTSGHVGVPACNYVKLEDVADMNYFTVNNEGEVCIKGTNVFK
GYLKDPEKTQEALDSDGWLHTGDIGRWLPNGTLKIIDRKKNIFKLAQGEYIAPEKIENIYNR
SQPVLQIFVHGESLRSSLVGVVVPD TDVLP SFAAKLG VKGSFEELCQNQVVREAILEDLQKI
GKESGLKTFEQVKAIFLHPEPF SIENGLLTPTL KAKRGELSKYFRTQIDSLYEHIQD

Important features:

Type II transmembrane domain:

amino acids 61-80

Putative AMP-binding domain signature.

amino acids 314-325

N-glycosylation site.

amino acids 102-105, 588-591 and 619-622

FIGURE 53

GGAGGCGGAGGCCGCGGCGAGCCGGGCGGAGCAGTGAGGGCCCTAGCGGGGCCCCGAGCGGGG
CCCCGGGGCCCCCTAAGCCATTCTCTGAAGTCATGGGCTGGCCAGGACATTGGTGACCCGCCAAT
CCGGTATGGACGACTGGAAGCCCAGCCCCCTCATCAAGCCCTTTGGGGCTCGGAAGAAGCGG
AGCTGGTACCTTACCTGGAAGTATAAACTGACAAACCAGCGGGCCCTGCGGAGATTCTGTCA
GACAGGGGCGGTGCTTTTCTGTGCTGGTGACTGTCATTGTCAATATCAAGTTGATCCTGGACA
CTCGGCGAGCCATCAGTGAAGCCAATGAAGACCCAGAGCCAGAGCAAGACTATGATGAGGCC
CTAGGCCGCTGGAGCCCCCACGGCGCAGAGGCAGTGGTCCCCGGCGGGTCCTGGACGTAGA
GGTGTATTCAAGTCGCAGCAAAGTATATGTGGCAGTGGATGGCACCACGGTGCTGGAGGATG
AGGCCCGGGAGCAGGGCCGGGGCATCCATGTCATTGTCTCAACCAGGCCACGGGCCACGTG
ATGGCAAACGTTGTGTTTGACACGTACTCACCTCATGAGGATGAGGCCATGGTGCTATTCTCT
CAACATGGTAGCGCCCCGGCCGAGTGCTCATCTGCACTGTCAAGGATGAGGGCTCCTTCCACC
TCAAGGACACAGCCAAGGCTCTGCTGAGGAGCCTGGGCAGCCAGGCTGGCCCTGCCCTGGGC
TGGAGGGACACATGGGCCTTCGTGGGACGAAAAGGAGGTCCTGTCTTCGGGGAGAAACATTTC
TAAGTCACCTGCCCTCTCTTCTGGGGGGACCCAGTCCTGCTGAAGACAGATGTGCCATTGA
GCTCAGCAGAAGAGGCAGAGTGCCACTGGGCAGACACAGAGCTGAACCGTCGCCGCCGGCGC
TTCTGCAGCAAAGTTGAGGGCTATGGAAGTGTATGCAGCTGCAAGGACCCACACCCATCGA
GTTCAGCCCTGACCCACTCCCAGACAACAAGTCTCAATGTGCCTGTGGCTGTCAATTGCAG
GGAACCGACCCAATTACCTGTACAGGATGCTGCGCTCTCTGCTTTCAGCCCAGGGGGTGTCT
CCTCAGATGATAACAGTTTTTCATTGACGGCTACTATGAGGAACCCATGGATGTGGTGCGCACT
GTTTGGTCTGAGGGGCATCCAGCATACTCCCATCAGCATCAAGAATGCCCGCGTGTCTCAGC
ACTACAAGGCCAGCCTCACTGCCACTTTCAACCTGTTTTCCGGAGGCCAAGTTTGCTGTGGTT
CTGGAAGAGGACCTGGACATTGCTGTGGATTTTTTTCAGTTTCCTGAGCCAATCCATCCACCT
ACTGGAGGAGGATGACAGCCTGTACTGCATCTCTGCCTGGAATGACCAGGGGTATGAACACA
CGGCTGAGGACCCAGCACTACTGTACCGTGTGGAGACCATGCCTGGGCTGGGCTGGGTGCTC
AGGAGGTCCTTGTAACAAGGAGGAGCTTGAGCCCAAGTGGCCTACACCGGAAAAGCTCTGGGA
TTGGGACATGTGGATGCGGATGCCTGAACAACGCCGGGGCCGAGAGTGATCATCCCTGACG
TTTCCCGATCCTACCACTTTGGCATCGTCGGCCTCAACATGAATGGCTACTTTCACGAGGCC
TACTTCAAGAAGCACAAAGTTCAACACGGTTCCAGGTGTCCAGCTCAGGAATGTGGACAGTCT
GAAGAAAGAAGCTTATGAAGTGGAAGTTCACAGGCTGCTCAGTGAGGCTGAGGTTCTGGACC
ACAGCAAGAACCCTTGTGAAGACTCTTTCCTGCCAGACACAGAGGGCCACACCTACGTGGCC
TTTATTTCGAATGGAGAAAGATGATGACTTCACCACCTGGACCCAGCTTGCCAAGTGCCTCCA
TATCTGGGACCTGGATGTGCGTGGCAACCATCGGGGCCTGTGGAGATTGTTTCGGAAGAAGA
ACCACTTCCTGGTGGTGGGGGTCCCGGCTTCCCCCTACTCAGTGAAGAAGCCACCCTCAGTC
ACCCCAATTTTCTGGAGCCACCCCCAAAGGAGGAGGGAGCCCCAGGAGCCCCAGAACAGAC
ATGAGACCTCCTCCAGGACCTGCGGGGCTGGGTACTGTGTACCCCCAGGCTGGCTAGCCCT
TCCCTCCATCCTGTAGGATTTTGTAGATGCTGGTAGGGGCTGGGGCTACCTTGTTTTTAACA
TGAGACTTAATTACTAACTCCAAGGGGAGGGTTCCCCTGCTCCAACACCCCGTTCTTGAGTT
AAAAGTCTATTTATTTACTTCTTGTGGAGAAGGGCAGGAGAGTACCTGGGAATCATTACG
ATCCCTAGCAGCTCATCCTGCCCTTTGAATACCCTCACTTTCCAGGCCTGGCTCAGAATCTA
ACCTATTTATTGACTGTCCTGAGGGCCTTGAAAACAGGCCGAACCTGGAGGGCCTGGATTTT
TTTTTGGGCTGGAATGCTGCCCTGAGGGTGGGGCTGGCTCTTACTCAGGAACTGCTGTGCC
CAACCCATGGACAGGCCAGCTGGGGCCCATGCTGACACAGACTCACTCAGAGACCCCTTA
GACACTGGACCAGGCCTCCTCTCAGCCTTCTCTTTGTCCAGATTTCCAAAGCTGGATAAGTT
GGTCATTGATTAAAAAAGGAGAAGCCCTCTGGGAAAAA

FIGURE 54

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA61185

><subunit 1 of 1, 660 aa, 1 stop

><MW: 75220, pI: 6.76, NX(S/T): 0

MDDWKPSPLIKPFGARKKRSWYLTWKYKLTNQALRRFCQTGAVLFLLVTVIVNIKLILDTR
RAISEANEDPEPEQDYDEALGRLEPPRRRGSGPRRVLDVEVYSSRSKVYVAVDGTTVLEDEA
REQGRGIHVIVLNQATGHVMAKRVFDTYSPHEDEAMVLFLNMVAPGRVLICTVKDEGSFHLK
DTAKALLRSLGSQAGPALGWRDTWAFVGRKGGPVFGEKHSKSPALSSWGDPVLLKTDVPLSS
AEEAECHWADTELNRNRRRRRFC SKVEGYGSVCCKDPTPIEFSPDPLDNKVLNVPVAVIAGN
RPNYLYRMLRSLLSAQGVSPQMITVFIDGYEPM DVVALFGLRGIQHTPISIKNARVSQHY
KASLTATFNLFPFAKFAVVLEEDLDIAVDFFSFLSQSIHLLEEDDSLYCISAWNDQGYEHTA
EDPALLYRVETMPGLGWVLRRSLYKEELEPKWPTPEKLWDWDMWMRMPEQRRGRECIIPDVS
RSYHFGIVGLNMNGYFHEAYFKKHKFNTVPGVQLRNVD SLKKEAYEVEVHRLLSEAEVLDHS
KNPCEDSFLPDTEGHTYVAFIRMEKDDDFTTWTQLAKCLHIWDL DVRGNHRGLWRLFRKKNH
FLVVGVPASPYSVKKPPSVTPIFLEPPPKEEGAPGAPEQT

Important features of the protein:

Transmembrane domain:

amino acids 38-55

Homologous region to Mouse GNT1

amino acids 229-660

FIGURE 55

CGGACGCGTGGGCTGCTGGTGGGAAGGCCTAAAGAACTGGAAAGCCCACTCTCTTGGAACCACCACAC
CTGTTTAAAGAACCTAAGCACCATTTAAAGCCACTGGAAATTTGTTGTCTAGTGGTTGTGGGTGAATA
AAGGAGGGCAGAAATGGATGATTTTCATCTCCATTAGCCTGCTGTCTCTGGCTATGTTGGTGGGATGTTA
CGTGGCCGGAATCATTCCCTTGGCTGTTAATTTCTCAGAGGAACGACTGAAGCTGGTGAAGTGTGTTTGG
GTGCTGGCCTTCTCTGTGGAAGTCTCTGGCAGTCATCGTGCCTGAAGGAGTACATGCCCTTTATGAA
GATATTCTTGAGGGAAAACACCACCAAGCAAGTGAAACACATAATGTGATTGCATCAGACAAAGCAGC
AGAAAAATCAGTTGTCCATGAACATGAGCACAGCCACGACCACACACAGCTGCATGCCCTATATTGGTG
TTTCCCTCGTTCTGGGCTTCGTTTTTCATGTTGCTGGTGGACCAGATTGGTAACTCCCATGTGCATTCT
ACTGACGATCCAGAAGCAGCAAGGTCTAGCAATTCAAAATCACCACCACGCTGGGTCTGGTTGTCCA
TGCTGCAGCTGATGGTGTGCTTTGGGAGCAGCAGCATCTACTTCACAGACCAGTGTCCAGTTAATTG
TGTTTGTGGCAATCATGCTACATAAGGCACCAGCTGCTTTTGGACTGGTTTCCTTCTTGATGCATGCT
GGCTTAGAGCGGAATCGAATCAGAAAGCACTTGCTGGTCTTTGCATTGGCAGCACCAGTTATGTCCAT
GGTGACATACTTAGGACTGAGTAAGAGCAGTAAAGAAGCCCTTTCAGAGGTGAACGCCACGGGAGTGG
CCATGCTTTTCTCTGCCGGGACATTTCTTTATGTTGCCACAGTACATGTCCTCCCTGAGGTGGGCGGA
ATAGGGCACAGCCACAAGCCCGATGCCACGGGAGGGAGAGGCCCTCAGCCGCCTGGAAGTGGCAGCCCT
GGTCTGGGTGTCCTCATCCCTCTCATCCTGTCAGTAGGACACCAGCATTAATGTTCAAGGTCCAGC
CTTGGTCCAGGGCCGTTTGCCATCCAGTGAGAACAGCCGGCACGTGACAGCTACTCACTTCCTCAGTC
TCTTGTCTCACCTTGCGCATCTCTACATGTATTCTTAGAGTCCAGAGGGGAGGTGAGGTTAAACCTG
AGTAATGGAAAAGCTTTTAGAGTAGAAACACATTTACGTTGCAGTTAGCTATAGACATCCCATTGTGT
TATCTTTTAAAGGCCCTTGACATTTTGCGTTTTAATATTTCTCTTAACCCTATTCTCAGGGAAGATG
GAATTTAGTTTTAAGGAAAAGAGGAGAAGTTCATACTCACAATGAAATAGTGATTATGAAAATACAGT
GTTCTGTAATTAAGCTATGTCTCTTTCTTCTTAGTTTAGAGGCTCTGCTACTTTATCCATTGATTTTT
AACATGGTTCCCACCATGTAAGACTGGTGTCTTTAGCATCTATGCCACATGCGTTGATGGAAGGTCATA
GCACCCACTCACTTAGATGCTAAAGGTGATTCTAGTTAATCTGGGATTAGGGTCAGGAAAATGATAGC
AAGACACATTGAAAGCTCTCTTTATACTCAAAGAGATATCCATTGAAAAGGGATGTCTAGAGGGATT
TAAACAGCTCCTTTGGCACGTGCCTCTCTGAATCCAGCCTGCCATTCCATCAAATGGAGCAGGAGAGG
TGGGAGGAGCTTCTAAAGAGGTGACTGGTATTTTGTAGCATTCCCTTGTCAAGTTCTCCTTTGCAGAAT
ACCTGTCTCCACATTCTTAGAGAGGAGCCAAGTTCTAGTAGTTTCAGTTCTAGGCTTTCCTTCAAGAA
CAGTCAGATCACAAAGTGTCTTTGGAAATTAAGGGATATTAAATTTTAAGTGATTTTGGATGGTTAT
TGATATCTTTGTAGTAGCTTTTTTTTAAAGACTACCAAATGTATGGTTGTCCTTTTTTTTTTGT
TTTTTTTTTAATTATTTCTCTTAGCAGATCAGCAATCCCTCTAGGGACCTAAATACTAGGTCAGCTTT
GGCGACACTGTGTCTTCTCACATAACCACCTGTAGCAAGATGGATCATAAATGAGAAGTGTTTGCCTA
TTGATTTAAAGCTTATTGGAATCATGTCTCTTGTCTCTTCGTCTTTTCTTTGCTTTTCTTCTAACTTT
TCCCTCTAGCCTCTCCTCGCCACAATTTGCTGCTTACTGCTGGTGTAAATATTTGTGTGGGATGAATT
CTTATCAGGACAACCACTTCTCGAAGTGTAAATGAAGATAATAATATCTTTATTCTTTATCCCCTT
CAAAGAAATTACCTTTGTGTCAAATGCCGCTTTGTTGAGCCCTTAAATACCACCTCCTCATGTGTAA
ATTGACACAATCACTAATCTGGTAATTTAAACAATTGAGATAGCAAAAGTGTTTAACAGACTAGGATA
ATTTTTTTTTTCATATTTGCCAAAATTTTGTAAACCCTGTCTTGTCAAATAAGTGTATAATATTGTAT
TATTAATTTATTTTACTTTCTATAACATTTCAAACACATTACACTAAGGGGGAACCAAGACTAGTT
TCTTCAGGGCAGTGGACGTAGTAGTTTGTAAAAACGTTTTCTATGACGCATAAGCTAGCATGCCTATG
ATTTATTTCTTTCATGAATTTGTCACTGGATCAGCAGCTGTGGAAATAAAGCTTGTGAGCCCTCTGCT
GGCCACAGTGAGGAAAGTAGCACAAATAGGATACAGTTGTATGTAGTCATTGGCAACAATTGCATACA
ATTTTACTACCAAGAGAAGGTATAGTATGGAAAGTCCAAATGACTTCCTTGATTGGATGTAAACAGCT
GACTGGTGTGAGACTTGAGGTTTCATCTAGTCCTTCAAACCTATATGGTTGCCTAGATTCTCTCTGGA
AACTGACTTTGTCAAATAAATAGCAGATTGTAGTGTCAAAAAAA

FIGURE 56

MDDFISISLLSLAMLVGCYVAGIIP LAVNFSEERLKLVTVLGAGLLCGTALAVIVPEGVHAL
YEDILEGKHHQASETHNVIASDKAAEKSVVHEHEHSHDHTQLHAYIGVSLVLGFVFMLLVDQ
IGNSHVHSTDDPEAARSSNSKITTTTLGLVVHAAADGVALGAAASTSQTSVQLIVFVAIMLHK
APAAFGLVSFLMHAGLERNRIRKHL LVFALAAPVMSMVTYLGLSKSSKEALSEVNATGVAML
FSAGTFLYVATVHVLPEVGGIGHSHKPDATGGRGLSRLEVAALVLGCLIP LILSVGHQH

Signal peptide:

amino acids 1-18

Transmembrane domain:

amino acids 37-56, 106-122, 211-230, 240-260, 288-304

FIGURE 57

GCTCGAGGCCGGCGGCGGGAGAGCGACCCGGGCGGCCTCGTAGCGGGGCCCCGGATCCC
CGAGTGGCGGCCGGAGCCTCGAAAAGAGATTCTCAGCGCTGATTTTGAGATGATGGGCTTGG
GAAACGGGCGTCGCAGCATGAAGTCGCCGCCCTCGTGCTGGCCGCCCTGGTGGCCTGCATC
ATCGTCTTGGGCTTCAACTACTGGATTGCGAGCTCCCGGAGCGTGGACCTCCAGACACGGAT
CATGGAGCTGGAAGGCAGGGTCCGCAGGGCGGCTGCAGAGAGAGGGCGCCGTGGAGCTGAAGA
AGAACGAGTTCCAGGGAGAGCTGGAGAAGCAGCGGGAGCAGCTTGACAAAATCCAGTCCAGC
CACAACCTTCCAGCTGGAGAGCGTCAACAAGCTGTACCAGGACGAAAAGGCGGTTTTTGGTGAA
TAACATCACCACAGGTGAGAGGCTCATCCGAGTGCTGCAAGACCAGTTAAAGACCCTGCAGA
GGAATTACGGCAGGCTGCAGCAGGATGTCCTCCAGTTTCAGAAGAACCAGACCAACCTGGAG
AGGAAGTTCTCCTACGACCTGAGCCAGTGTCATCAATCAGATGAAGGAGGTGAAGGAACAGTG
TGAGGAGCGAATAGAAGAGGTCACCAAAAAGGGGAATGAAGCTGTAGCTTCCAGAGACCTGA
GTGAAAACAACGACCAGAGACAGCAGCTCCAAGCCCTCAGTGAGCCTCAGCCCAGGCTGCAG
GCAGCAGGCCTGCCACACACAGAGGTGCCACAAGGGAAGGGAAACGTGCTTGGTAACAGCAA
GTCCCAGACACCAGCCCCCAGTTCCGAAGTGGTTTTTGGATTCAAAGAGACAAGTTGAGAAAG
AGGAAACCAATGAGATCCAGGTGGTGAATGAGGAGCCTCAGAGGGACAGGCTGCCGCAGGAG
CCAGGCCGGGAGCAGGTGGTGGAAAGACAGACCTGTAGGTGGAAGAGGCTTCGGGGGAGCCGG
AGAACTGGGCCAGACCCACAGGTGCAGGCTGCCCTGTCAGTGAGCCAGGAAAATCCAGAGA
TGGAGGGCCCTGAGCGAGACCAGCTTGTCATCCCCGACGGACAGGAGGAGGAGCAGGAAGCT
GCCGGGGAAGGGAGAAACCAGCAGAACTGAGAGGAGAAGATGACTACAACATGGATGAAAA
TGAAGCAGAATCTGAGACAGACAAGCAAGCAGCCCTGGCAGGGAATGACAGAAACATAGATG
TTTTTAATGTTGAAGATCAGAAAAGAGACACCATAAATTTACTTGATCAGCGTGAAAAGCGG
AATCATACACTCTGAATTGAACTGGAATCACATATTTCAACAACAGGGCCGAAGAGATGACTA
TAAAATGTTTCATGAGGGACTGAATACTGAAAACGTGAAATGTACTAAATAAAATGTACATCTGA

FIGURE 58

MMGLGNRRSMKSPPLVLAALVACIIVLGFNYWIASRSVDLQTRIMELEGRVRRAAAERGA
VELKKNEFQGELEKQREQLDKIQSSHNFQLESVNKLYQDEKAVLVNNITTGERLIRVLQDQL
KTLQRNYGRLQQDVLQFQKNQTNLERKFSYDLSQCINQMKEVKEQCEERIEEVTKKGNEAVA
SRDLSENNDQRQQQLQALSEPQPRQLQAAGLPHTTEVPQGKGNVLGNSKSQTPAPSSEVVLDSKR
QVEKEETNEIQVVNEEPQRDRLPQEPGREQVVEDRPVGGRGFGGAGELGQTPQVQAALSVSQ
ENPEMEGPERDQLVIPDGQEEEQEAAGEGRNQOKLRGEDDYNMDENEAESETDKQAALAGND
RNIDVFNVEDQKRDTINLLDQREKRNHTL

Signal peptide:

amino acids 1-29

FIGURE 59

GGATGCAGAAAGCCTCAGTGTGCTCTTCCTGGCCTGGGTCTGCTTCCTCTTCTACGCTGGCATTGCCCTCTTCA
CCAGTGGCTTCCTGCTCACCCTGTTGGAGCTCACCACCATAGCAGCTGCCAAGAGCCCCAGGCCCTGGGTCCC
TGCCATGGGGGAGCCAAGGGAAACCTGGGGCTGCTGGATGGCTTCCCGATTTTCGCGGGTGTGTTGGTGCTGA
TAGATGCTCTGCGATTTGACTTCGCCCAGCCCCAGCATTACACAGTGCCTAGAGAGCCTCCTGTCTCCCTACCCT
TCCTGGGCAAACCTAAGCTCCTTGAGAGGATCCTGGAGATTAGCCCCACCATGCCCGGCTCTACCGATCTCAGG
TTGACCCTCCTACCACCACCATGCAGCGCCTCAAGGCCCTCACCCTGCTCAGTGCCTACCTTTATTGATGCTG
GTAGTAACCTCGCCAGCCACGCCATAGTGAAGACAATCTCATTAAGCAGCTCACCAGTGCAGGAAGGCGTGTAG
TCTTCATGGGAGATGATACCTGGAAAGACCTTTTCCCTGGTGCTTTCTCCAAAGCTTTCTTCTTCCCATCCTTCA
ATGTCAGAGACCTAGACACAGTGGACAATGGCATCCTGGAACACCTCTACCCCACCATGGACAGTGGTGAATGGG
ACGTGCTGATTGCTCACTTCCTGGGTGTGGACCACTGTGGCCACAAGCATGGCCCTCACCACCCTGAAATGGCCA
AGAACTTAGCCAGATGGACCAGGTGATCCAGGGACTTGTGGAGCGTCTGGAGAATGACACACTGCTGGTAGTGG
CTGGGGACCATGGGATGACCACAAATGGAGACCATGGAGGGGACAGTGAGCTGGAGGTCTCAGCTGCTCTCTTTC
TGTATAGCCCCACAGCAGTCTTCCCCAGCACCCCCACAGAGGAGCCAGAGGTGATTCTCAAGTTAGCCTTGTGC
CCACGCTGGCCCTGCTGCTGGGCCTGCCATCCCATTTGGGAATATCGGGGAAGTGATGGCTGAGCTATTCTCAG
GGGTGAGGACTCCAGCCCCACTCCTCTGCTTTAGCCCAAGCCTCAGCTCTCCATCTCAATGCTCAGCAGGTGT
CCCGATTTCTTCATACCTACTCAGCTGCTACTCAGGACCTTCAAGCTAAGGAGCTTCATCAGCTGCAGAACCTCT
TCTCCAAGGCCCTCTGCTGACTACCAGTGGCTTCTCCAGAGCCCCAAGGGGGCTGAGGCGACACTGCCGACTGTGA
TTGCTGAGCTGCAGCAGTTCCTGCGGGGAGCTCGGGCCATGTGCATCGAGTCTTGGGCTCGTTTCTCTCTGGTCC
GCATGGCGGGGGGTACTGCTCTCTTGGCTGCTTCTGCTTTATCTGCCTGCTGGCATCTCAGTGGGCAATATCCC
CAGGCTTTCCATTCTGCCCTCTACTCCTGACACCTGTGGCCTGGGGCCTGGTGGGGCCATAGCGTATGCTGGAC
TCCTGGGAACTATTGAGCTGAAGCTAGATCTAGTGCTTCTAGGGGCTGTGGCTGCAGTGAGCTCATTCCTCCCTT
TTCTGTGGAAAGCCTGGGCTGGCTGGGGGTCCAAGAGGCCCTGGCAACCCTGTTTCCCATCCCTGGGCCCGTCC
TGTTACTCCTGCTGTTTTGCTTGGCTGTGTTCTTCTCTGATAGTTTTGTGTGTAGCTGAGGCCAGGGCCACCCCT
TCCTTTTGGGCTCATTCATCCTGCTCCTGGTGTGTCAGCTTCACTGGGAGGGCCAGCTGCTTCCACCTAAGCTAC
TCACAATGCCCCGCCTTGGCACTTCAGCCACAACAAACCCCCACGGCACAATGGTGCATATGCCCTGAGGCTTG
GAATTGGGTTGCTTTTATGTACAAGGCTAGCTGGGCTTTTTCATCGTTGCCCTGAAGAGACACCTGTTTGCCACT
CCTCTCCCTGGCTGAGTCTCTGGCATCCATGGTGGGTGGTTCGAGCCAAGAATTTATGGTATGGAGCTTGTGTGG
CGGCGCTGGTGGCCCTGTTAGCTGCCGTGCGCTTGTGGCTTCGCGCTATGGTAATCTCAAGAGCCCCGAGCCAC
CCATGCTCTTTGTGCGCTGGGGACTGCCCTAATGGCATTGGGTACTGCTGCCTACTGGGCATTGGCGTGGGGG
CAGATGAGGCTCCCCCGTCTCCGGGTCTGGTCTCTGGGGCATCCATGGTGTGCTGCCTCGGGCTGTAGCAGGGC
TGGCTGCTTCAGGGCTCGCGCTGCTGCTCTGGAAGCCTGTGACAGTGTGCTGGTGAAGGCTGGGGCAGGCGCTCCAA
GGACCAGGACTGTCTCACTCCCTTCTCAGGCCCCCCCCACTTCTCAAGCTGACTTGGATTATGTGGTCCCTCAA
TCTACCGACACATGCAGGAGGAGTTCGCGGGCCGGTTAGAGAGGACCAAATCTCAGGGTCCCCCTGACTGTGGCTG
CTTATCAGTTGGGGAGTGTCTACTCAGCTGCTATGGTACAGCCCTCACCCTGTTGGCCTTCCCCTTCTGCTGT
TGATGCGGAGCGCATCAGCCTTGTGTTCTGCTTCTGTTTCTGCAGAGCTTCCTTCTCCTACATCTGCTTGTG
CTGGGATACCCGTCACCACCCCTGGTCTTTTACTGTGCCATGGCAGGCACTCTCGGCTTGGGCCCTCATGGCCA
CACAGACCTTCTACTCCACAGGCCACCAGCCTGTCTTTCCAGCCATCCATTGGCATGCAGCCTTCGTGGGATTCC
CAGAGGGTTCATGGCTCCTGTACTTGGCTGCCTGCTTTGCTAGTGGGAGCCAACACCTTGCCTCCCACCTCCTCT
TTGCAGTAGGTTGCCCACTGCTCCTGCTCTGGCCTTTCTGTGTGAGAGTCAAGGGCTGCGGAAGAGACAGCAGC
CCCCAGGGAATGAAGCTGATGCCAGAGTCAGACCCGAGGAGGAAGAGGAGCCACTGATGGAGATGCGGCTCCGGG
ATGCGCCTCAGCACTTCTATGCAGCACTGCTGCAGCTGGGCCTCAAGTACCTCTTTATCCTTGGTATTTCAGATTC
TGGCCTGTGCTTGGCAGCCTCCATCCTTCGCAGGCATCTCATGGTCTGGAAGTGTTTTGCCCTAAGTTTCATAT
TTGAGGCTGTGGGCTTCATTGTGAGCAGCGTGGGACTTCTCCTGGGCATAGCTTTGGTGATGAGAGTGGATGGTG
CTGTGAGCTCCTGGTTCAGGCAGCTATTTCTGGCCAGCAGAGGTAGCCTAGTCTGTGATTACTGGCACTTGGCT
ACAGAGAGTGTGGAGAACAGTGTAGCCTGGCCTGTACAGGTACTGGATGATCTGCAAGACAGGCTCAGCCATAC
TCTTACTATCATGCAGCCAGGGGCCGCTGACATCTAGGACTTCATTATTCTATAATTACAGGACCACAGTGGAGTA
TGATCCCTAACTCCTGATTGGATGCATCTGAGGGACAAGGGGGCGGTCTCCGAAGTGGAATAAAATAGGCCGG
GCGTGGTGAATGACCTATAATCCAGCACTTTGGGAGGCAGAGGTGGGAGGATTGCTTGGTCCCAGGAGTTCA
AGACCAGCCTGTGGAACATAACAAGACCCCGTCTCTACTATTTAAAAAAAGTGTAATAAAATGATAATAT

FIGURE 60

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA62809

<subunit 1 of 1, 1089 aa, 1 stop

<MW: 118699, pI: 8.49, NX(S/T): 2

MQKASVLLFLAWVCFLFYAGIALFTSGFLLTRLELTNHSSCQEPPGPGSLPWGSQGKPGACW
MASRFSRVVLVLIDALRFDFAQPQHSHVPREPPVSLPFLGKLSSLQRILEIQPHHARLYRSQ
VDPPTTTMQRKALTGSLPTFIDAGSNFASHAIVEDNLIKQLTSAGRRVFMGDDTWKDLF
PGAFSKAFFFPFNFVRDLDTVDNGILEHLYPTMDSGEWDVLI AHFLGVDHCGHKHGP HHPEM
AKKLSQMDQVIQGLVERLENDTLLVVAGDHGMTTNGDHGGDSELEVSAALFLYSPTAVFPST
PPEEPEVIPQVSLVPTLALLLGLPIPFGNIGEVM AELFSGGEDSQPHSSALAQASALHLNAQ
QVSRFLHTYSAATQDLQAKELHQLQNLFSKASADYQWLLQSPKGAEATLPTVIAELQQFLRG
ARAMCIESWARFSLVRMAGGTALLAASCFICLLASQWAI SPGF PFCPLLLTPVAWGLVGAI A
YAGLLGTIELKLDLVLLGAVAAVSSFLPFLWKAWAGWGSKRPLATLFPPIPGPVLLLLLLFRLA
VFFSDSFVVAEARATPFLLG SFILLLVVQLHWEGQLLPKLLTMPRLGTSATTNPPRHNGAY
ALRLGIGLLLCTRLAGLFHRCPEETPVCHSSPWLSPLASMVGGRAKNLWYGACVAALVALLA
AVRLWLRRYGNLKSPEPPMLFVRWGLPLMALGTAAYWALASGADEAPPRLRVLVSGASMVLP
RAVAGLAASGLALLLWKPVTVLVKAGAGAPRTRTVLTPFSGPPTSQADLDYVVPQIYRHMQE
EFRGRLERTKSQGPLTVAAYQLGSVYSAAMVTALTLLAFPLLLLHAERISLVFLLLFLQSFL
LLHLLAAGIPVTTTPGPFTVPWQAVSAWALMATQTFYSTGHQPVFPAIHWHA AFVGFPEGHGS
CTWLPALLVGANTFASHLLFAVGCPLLLLWPFLCESQGLRKRQQPPGNEADARVRPEEEEEEP
LMEMRLRDAPQHFYAALLQLGLKYLFI LGI QILACALAASILRRHLMVWKVFAPKFIFEAVG
FIVSSVGLLLGIALVMRVDGAVSSWFRQLFLAQQR

Important features:

Signal peptide:

amino acids 1-16

Transmembrane domains:

amino acids 317-341, 451-470, 481-500, 510-527, 538-555, 831-850,
1016-1034, 1052-1070

Leucine zipper pattern.

amino acids 843-864

N-glycosylation sites.

amino acids 37-40, 268-271

FIGURE 61

TGCCGCTGCCGCCGCTGCTGCTGTTGCTCCTGGCGGCGCCTTGGGGACGGGCAGTTCCTGT
GTCTCTGGTGGTTTGCCTAAACCTGCAAACATCACCTTCTTATCCATCAACATGAAGAATGT
CCTACAATGGACTCCACCAGAGGGTCTTCAAGGAGTTAAAGTTACTTACACTGTGCAGTATT
TCATCACAAATTGGCCCACCAGAGGTGGCACTGACTACAGATGAGAAGTCCATTTCTGTTGT
CCTGACAGCTCCAGAGAAGTGGAAGAGAAATCCAGAAGACCTTCCTGTTTCCATGCAACAAA
TATACTCCAATCTGAAGTATAACGTGTCTGTGTTGAATACTAAATCAAACAGAACGTGGTCC
CAGTGTGTGACCAACCACACGCTGGTGCTCACCTGGCTGGAGCCGAACACTCTTTACTGCGT
ACACGTGGAGTCCTTCGTCCCAGGGCCCCCTCGCCGTGCTCAGCCTTCTGAGAAGCAGTGTG
CCAGGACTTTGAAAGATCAATCATCAGAGTTCAAGGCTAAAATCATCTTCTGGTATGTTTTG
CCCATATCTATTACCGTGTTTCTTTTTTCTGTGATGGGCTATTCCATCTACCGATATATCCA
CGTTGGCAAAGAGAAACACCCAGCAAATTTGATTTTGATTTATGGAAATGAATTTGACAAAA
GATTCTTTGTGCCTGCTGAAAAAATCGTGATTAACCTTTATCACCTCAATATCTCGGATGAT
TCTAAAATTTCTCATCAGGATATGAGTTTACTGGGAAAAAGCAGTGATGTATCCAGCCTTAA
TGATCCTCAGCCCAGCGGGAACCTGAGGCCCCCTCAGGAGGAAGAGGAGGTGAAACATTTAG
GGTATGCTTCGCATTTGATGGAAATTTTTTGTGACTCTGAAGAAAACACGGAAGGTACTTCT
CTCACCCAGCAAGAGTCCCTCAGCAGAACAAATACCCCCGGATAAAACAGTCATTGAATATGA
ATATGATGTCAGAACCACTGACATTTGTGCGGGGCCTGAAGAGCAGGAGCTCAGTTTGCAGG
AGGAGGTGTCCACACAAGGAACATTATTGGAGTCGCAGGCAGCGTTGGCAGTCTTGGGCCCCG
CAAACGTTACAGTACTCATAACCCCTCAGCTCCAAGACTTAGACCCCTGGCGCAGGAGCA
CACAGACTCGGAGGAGGGGCGGAGGAAGAGCCATCGACGACCCTGGTCGACTGGGATCCCC
AAACTGGCAGGCTGTGTATTCCTTCGCTGTCCAGCTTCGACCAGGATTCAGAGGGCTGCGAG
CCTTCTGAGGGGGATGGGCTCGGAGAGGAGGGTCTTCTATCTAGACTCTATGAGGAGCCGGC
TCCAGACAGGCCACCAGGAGAAAATGAAACCTATCTCATGCAATTCATGGAGGAATGGGGGT
TATATGTGCAGATGGAAAACTGATGCCAACACTTCCTTTTGCCTTTTGTTCCTGTGCAAAC
AAGTGAGTCACCCCTTTGATCCCAGCCATAAAGTACCTGGGATGAAAGAAGTTTTTTCCAGT
TTGTCAGTGTCTGTGAGAATTACTTATTTCTTTTCTTATTCTCATAGCACGTGTGTGATTG
GTTTCATGCATGTAGGTCTCTTAACAATGATGGTGGGCCTCTGGAGTCCAGGGGCTGGCCGGT
TGTTCTATGCAGAGAAAGCAGTCAATAAATGTTTGCCAGACTGGGTGCAGAAATTTATTCAGG
TGGGTGT

FIGURE 62

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA62815

<subunit 1 of 1, 442 aa, 1 stop

<MW: 49932, pI: 4.55, NX(S/T): 5

MSYNGLHQRVFKELKLLTLCSISSQIGPPEVALTTDEKSISVVLTAPEKWKRNPEDLPVSMQ
QIYSNLKYNVSVLNTKSNRTWSQCVTNHTLVLTWLEPNTLYCVHVESFVPGPPRAQPSEKQ
CARTLKDQSSEFKAKIIFWYVLPISITVFLFSVMGYSIYRYIHVGKEKHPANLILYGNED
KRFFVPAEKIVINFITLNISSDKISHQDMSLLGKSSDVSSLNDPQPSGNLRPPQEEEEVKH
LGYASHLMEIFCDSEENTEGTSLTQQESLSRTIPDKTVIEWEYDVRTTDCAGPEEQELSL
QEEVSTQGTLLSQAALAVLGPQTLQYSYTPQLQDLDPLAQEHTDSEEGPEEEPSTTLVDWD
PQTGRLCIPSLSSFDQDSEGCEPSEGDLGEEGLLSRLYEAPDRPPGENETYLMQFMEEW
GLYVQMEN

Important features:

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 140-163

N-glycosylation sites.

amino acids 71-74, 80-83, 89-92, 204-207, 423-426

FIGURE 63

CGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGTCTCTGCGGGGAGACGCCAGCCTGCG
TCTGCCATGGGGCTCGGGTTGAGGGGCTGGGGACGTCTCTGCTGACTGTGGCCACCGCCCT
GATGCTGCCCCGTGAAGCCCCCGCAGGCTCCTGGGGGGGCCAGATCATCGGGGGGCCACGAGG
TGACCCCCCACTCCAGGCCCTACATGGCATCCGTGCGCTTCGGGGGGCCAACATCACTGCGGA
GGCTTCCTGCTGCGAGCCCGCTGGGTGGTCTCGGCCGCCCACTGCTTCAGCCACAGAGACCT
CCGCACTGGCCTGGTGGTGGTGGGCGCCACGTCCTGAGTACTGCGGAGCCCACCCAGCAGG
TGTTTGGCATCGATGCTCTCACCACGCACCCCGACTACCACCCCATGACCCACGCCAACGAC
ATCTGCCTGCTGCGGCTGAACGGCTCTGCTGTCTGGGCCCTGCAGTGGGGCTGCTGAGGCT
GCCAGGGAGAAGGGGCCAGGCCCCCCACAGCGGGGACACGGTGCCGGGTGGCTGGCTGGGGCT
TCGTGTCTGACTTTGAGGAGCTGCCGCCTGGACTGATGGAGGCCAAGGTCCGAGTGCTGGAC
CCGGACGTCTGCAACAGCTCCTGGAAGGGCCACCTGACACTTACCATGCTCTGCACCCGCAG
TGGGGACAGCCACAGACGGGGCTTCTGCTCGGCCGACTCCGGAGGGCCCCCTGGTGTGCAGGA
ACCGGGCTCACGGCCTCGTTTCCTTCTCGGGCCTCTGGTGCGGCGACCCCAAGACCCCGAC
GTGTACACGCAGGTGTCCGCCTTTGTGGCCTGGATCTGGGACGTGGTTCGGCGGAGCAGTCC
CCAGCCCGGCCCCCTGCCTGGGACCACCAGGCCCCCAGGAGAAGCCGCCTTGAGCCACAACCT
TGCGGCATGCAAATGAGATGGCCGCTCCAGGCCTGGAATGTTCCGTGGCTGGGCCCCACGGG
AAGCCTGATGTTTCAGGGTTGGGGTGGGACGGGCAGCGGTGGGGCACACCCATTCCACATGCA
AAGGGCAGAAGCAAACCCAGTAAAATGTTAACTGACAAAAAAAAAAAAAAAAAAAAAGAAA

FIGURE 64

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA62845

><subunit 1 of 1, 283 aa, 1 stop

><MW: 30350, pI: 9.66, NX(S/T): 2

MGLGLRGWGRPLLTVATALMLPVKPPAGSWGAIIGGHEVTPHSRPYMASVRFGGQHHCGGF
LLRARWVVSAAHCFSHRDLRTGLVVLGAHVLSTAEP TQQVFGIDALTTHPDYHPMTHANDIC
LLRLNGSAVLGPAVGLLRLPGRRARPPTAGTRCRVAGWGFVSDFEELPPGLMEAKVRVLDPD
VCNSSWKGHLTLTMLCTRSGDSHRRGFCSADSGGPLVCRNRAHGLVSFSGLWCGDPKTPDVY
TQVSAFVAWIWDVVRSSPQPGPLPGTTRPPGEAA

Signal peptide:

amino acids 1-30

FIGURE 65

GAGCTACCCAGGCGGCTGGTGTGCAGCAAGCTCCGCGCCGACTCCGGACGCCTGACGCCTGA
CGCCTGTCCCCGGCCCCGGCATGAGCCGCTACCTGCTGCCGCTGTCCGGCGCTGGGCACGGTAG
CAGGCGCCGCGCTGCTGCTCAAGGACTATGTCACCGGTGGGGCTTGCCCCAGCAAGGCCACC
ATCCCTGGGAAGACGGTCATCGTGACGGGCGCCAACACAGGCATCGGGAAGCAGACCGCCTT
GGAAGTGGCCAGGAGAGGAGGCAACATCATCCTGGCCTGCCGAGACATGGAGAAGTGTGAGG
CGGCAGCAAAGGACATCCGCGGGGAGACCCTCAATCACCATGTCAACGCCCGGCACCTGGAC
TTGGCTTCCCTCAAGTCTATCCGAGAGTTTGCAGCAAAGATCATTGAAGAGGAGGAGCGAGT
GGACATTCTAATCAACAACGCGGGTGTGATGCGGTGCCCCCACTGGACCACCGAGGACGGCT
TCGAGATGCAGTTTGGCGTTAACCACCTGGGTCACTTTCTCTTGACAACTTGCTGCTGGAC
AAGCTGAAAGCCTCAGCCCCCTTCGCGGATCATCAACCTCTCGTCCCTGGCCCATGTTGCTGG
GCACATAGACTTTGACGACTTGAACTGGCAGACGAGGAAGTATAACACCAAAGCCGCCTACT
GCCAGAGCAAGCTCGCCATCGTCCTCTTCACCAAGGAGCTGAGCCGGCGGCTGCAAGGCTCT
GGTGTGACTGTCAACGCCCTGCACCCCGGCGTGGCCAGGACAGAGCTGGGCAGACACACGGG
CATCCATGGCTCCACCTTCTCCAGCACCACTCGGGCCCATCTTCTGGCTGCTGGTCAAGA
GCCCCGAGCTGGCCGCCAGCCAGCACATACTGGCCGTGGCGGAGGAACTGGCGGATGTT
TCCGGAAAGTACTTCGATGGACTCAAACAGAAGGCCCGGCCCGAGGCTGAGGATGAGGA
GGTGGCCCCGAGGCTTTGGGCTGAAAGTGCCCGCCTGGTGGGCTTAGAGGCTCCCTCTGTGA
GGGAGCAGCCCCCTCCCCAGATAACTCTGGAGCAGATTTGAAAGCCAGGATGGCGCCTCCAG
ACCGAGGACAGCTGTCCGCCATGCCCGCAGCTTCCTGGCACTACCTGAGCCGGGAGACCCAG
GACTGGCGGCCCGCCATGCCCGCAGTAGGTTCTAGGGGGCGGTGCTGGCCGCAGTGGACTGGC
CTGCAGGTGAGCACTGCCCCGGGCTCTGGCTGGTTCCGTCTGCTCTGCTGCCAGCAGGGGAG
AGGGGCCATCTGATGCTTCCCCTGGGAATCTAACTGGGAATGGCCGAGGAGGAAGGGGCTC
TGTGCACTTGCAGGCCACGTGAGGAGAGCCAGCGGTGCCTGTCCGGGAGGGTTCCAAGGTGC
TCCGTGAAGAGCATGGGCAAGTTGTCTGACACTTGGTGGATTCTTGGGTCCCTGTGGGACCT
TGTGCATGCATGGTCCTCTCTGAGCCTTGGTTTCTTCAGCAGTGAGATGCTCAGAATAACTG
CTGTCTCCCATGATGGTGTGGTACAGCGAGCTGTTGTCTGGCTATGGCATGGCTGTGCCGGG
GGTGTTTGCTGAGGGCTTCCCTGTGCCAGAGCCCAGCCAGAGAGCAGGTGCAGGTGTCATCCC
GAGTTCAGGCTCTGCACGGCATGGAGTGGGAACCCACAGCTGCTGCTACAGGACCTGGGA
TTGCCTGGGACTCCCACCTTCCTATCAATTCTCATGGTAGTCCAACTGCAGACTCTCAAAC
TTGCTCATTT

FIGURE 66

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64842

><subunit 1 of 1, 331 aa, 1 stop

><MW: 35932, pI: 8.45, NX(S/T): 1

MSRYLLPLSALGTVAGAAVLLKDYVTGGACPSKATIPGKTVIVTGANTGIGKQTALELARRG
GNIILACRDMEKCEAAAKDIRGETLNHHVNARHLDLASLKSIREFAAKIIEEEERVLDILINN
AGVMRCPHWTTEDGFEMQFGVNHLLGHFLLTNLLLDKCLKASAPSRIINLSSLAHVAGHIDFDD
LNWQTRKYNTKAAYCQSKLAIVLFTKELSRRLQSGVTVNALHPGVARTELGRHTGIHGSTF
SSTTLGPFIWLLVKSPELAAQPSTYLAVAEELADVSGKYFDGLKQKAPAPEAEDEEVARRLW
AESARLVGLEAPSVREQPLPR

Signal peptide:

amino acids 1-17

FIGURE 67

GAAGTTCGCGAGCGCTGGCATGTGGTCCTGGGGCGCGGCTGGCGGGCGCTGCTGGCGGTGCTG
GCGCTCGGGACAGGAGACCCAGAAAGGGCTGCGGCTCGGGGCGACACGTTCTCGGCGCTGAC
CAGCGTGGCGCGCGCCCTGGCGCCCGAGCGCCGGCTGCTGGGGCTGCTGAGGCGGTACCTGC
GCGGGGAGGAGGCGCGGCTGCGGGACCTGACTAGATTCTACGACAAGGTACTTTCTTTGCAT
GAGGATTCAACAACCCCTGTGGCTAACCTCTGCTTGCATTTACTCTCATCAAACGCCTGCA
GTCTGACTGGAGGAATGTGGTACATAGTCTGGAGGCCAGTGAGAACATCCGAGCTCTGAAGG
ATGGCTATGAGAAGGTGGAGCAAGACCTTCCAGCCTTTGAGGACCTTGAGGGAGCAGCAAGG
GCCCTGATGCGGCTGCAGGACGTGTACATGCTCAATGTGAAAGGCCTGGCCCGAGGTGTCTT
TCAGAGAGTCACTGGCTCTGCCATCACTGACCTGTACAGCCCCAAACGGCTCTTTTCTCTCA
CAGGGGATGACTGCTTCCAAGTTGGCAAGGTGGCCTATGACATGGGGGATTATTACCATGCC
ATTCCATGGCTGGAGGAGGCTGTCAGTCTCTTCCGAGGATCTTACGGAGAGTGGAAGACAGA
GGATGAGGCAAGTCTAGAAGATGCCTTGGATCACTTGGCCTTTGCTTATTTCCGGGCAGGAA
ATGTTTTCGTGTGCCCTCAGCCTCTCTCGGGAGTTTCTTCTCTACAGCCCAGATAATAAGAGG
ATGGCCAGGAATGTCTTGAAATATGAAAGGCTCTTGGCAGAGAGCCCCAACACGTGGTAGC
TGAGGCTGTCATCCAGAGGCCCAATATACCCACCTGCAGACCAGAGACACCTACGAGGGGC
TATGTCAGACCCTGGGTTCACAGCCCACTCTCTACCAGATCCCTAGCCTCTACTGTTCTCTAT
GAGACCAATTCCAACGCCTACCTGCTGCTCCAGCCCATCCGGAAGGAGGTCATCCACCTGGA
GCCCTACATTGCTCTCTACCATGACTTCGTCAGTGAAGGCTCAGAGGCTCAGAAAATTAGAGAAC
TTGCAGAACCATGGCTACAGAGGTCAGTGGTGGCATCAGGGGAGAAGCAGTTACAAGTGGAG
TACCGCATCAGCAAAAGTGCCTGGCTGAAGGACACTGTTGACCCAAACTGGTGACCCTCAA
CCACCGCATTGCTGCCCTCACAGGCCTTGATGTCCGGCCTCCCTATGCAGAGTATCTGCAGG
TGGTGAAGTATGGCATCGGAGGACACTATGAGCCTCACTTTGACCATGCTACGTCACCAAGC
AGCCCCCTCTACAGAATGAAGTCAGGAAACCGAGTTGCAACATTTATGATCTATCTGAGCTC
GGTGGAGCTGGAGGAGCCACAGCCTTCATCTATGCCAACCTCAGCGTGCCTGTGGTTAGGA
ATGCAGCACTGTTTTGGTGGAACCTGCACAGGAGTGGTGAAGGGGACAGTGACACACTTCAT
GCTGGCTGTCCTGTCTGGTGGGAGATAAGTGGGTGGCCAACAAGTGGATACATGAGTATGG
ACAGGAATTCCGCAGACCCTGCAGCTCCAGCCCTGAAGACTGGAACTGTTGGCAGAGAGAAGC
TGGTGGAGTCCTGTGGCTTTCCAGAGAAGCCAGGAGCCAAAAGCTGGGGTAGGAGAGGAGAA
AGCAGAGCAGCCTCCTGGAAGAAGGCCTTGTGAGCTTTGTCTGTGCCTCGCAAATCAGAGGC
AAGGGAGAGGTTGTTACCAGGGGACACTGAGAATGTACATTTGATCTGCCCCAGCCACGGAA
GTCAGAGTAGGATGCACAGTACAAAGGAGGGGGGAGTGGAGGCCTGAGAGGGAAGTTTCTGG
AGTTCAGATACTCTCTGTTGGGAACAGGACATCTCAACAGTCTCAGGTTTCGATCAGTGGGTC
TTTTGGCACTTTGAACCTTGACCACAGGGACCAAGAAGTGGCAATGAGGACACCTGCAGGAG
GGGCTAGCCTGACTCCCAGAACTTTAAGACTTTCTCCCCACTGCCTTCTGCTGCAGCCCAAG
CAGGGAGTGTCCCCCTCCCAGAAGCATATCCCAGATGAGTGGTACATTATATAAGGATTTTT
TTTAAGTTGAAAACAACCTTTCTTTTCTTTTGTATGATGGTTTTTTTAAACACAGTCATTAAAA
ATGTTTATAAATCAAAA

FIGURE 68

MGPGARLAALLAVLALGTGDPERAAARGDTFSALTSVARALAPERRLGLLRRYLRGEEARL
RDLTRFYDKVLSLHEDSTTPVANPLLAFTLIKRLQSDWRNVVHSLEASENIRALKDGYEKVE
QDLPAFEDLEGAARALMRLQDVYMLNVKGLARGVFQRTGSAITDLYSPKRLFSLTGDDCFQ
VGKVAYDMGDYYHAIPWLEEAVSLFRGSYGEWKTEDEASLEDALDHLAFAYFRAGNVSCALS
LSREFLLYSPDNKRMAARNVLKYERLLAESPNHVVAEAVIQRPNI PHLQTRDTYEGLCQTLGS
QPTLYQIPSLYCSYETNSNAYLLLQPIRKEVIHLEPYIALYHDFVSDSEAQKIRELAEPWLQ
RSVVASGEKQLQVEYRISKSAWLKDTVDPKLVTLNHRIAALTGLDVRPPYAEYLQVVNYGIG
GHYEPHFDHATSPSSPLYRMKSGNRVATFMIYLSSVEAGGATAFIYANLSVPVVRNAALFWW
NLHRSGEGDSDTLHAGCPVLVGDKWVANKWIHEYGQEFRRPCSSSPED

Signal peptide:

amino acids 1-19

FIGURE 69

GAGATAGGGAGTCTGGGTTTAAAGTTCCTGCTCCATCTCAGGAGCCCCTGCTCCCACCCCTAG
GAAGCCACCAGACTCCACGGTGTGGGGCCAATCAGGTGGAATCGGCCCTGGCAGGTGGGGCC
ACGAGCGCTGGCTGAGGGACCGAGCCGGAGAGCCCCGGAGCCCCCGTAACCCGCGCGGGGAG
CGCCCAGGATGCCGCGCGGGGACTCGGAGCAGGTGCGCTACTGCGCGCGCTTCTCCTACCTC
TGGCTCAAGTTTTCACTTATCATCTATTCCACCGTGTTCTGGCTGATTGGGGCCCTGGTCCT
GTCTGTGGGCATCTATGCAGAGGTTGAGCGGCAGAAATATAAAACCCTTGAAAGTGCCTTCC
TGGCTCCAGCCATCATCCTCATCCTCCTGGGCGTCGTCATGTTTCATGGTCTCCTTCATTGGT
GTGCTGGCGTCCCTCCGTGACAACCTGTACCTTCTCCAAGCATTCATGTACATCCTTGGGAT
CTGCCTCATCATGGAGCTCATTGGTGGCGTGGTGGCCTTGACCTTCCGGAACCAGACCATTG
ACTTCCTGAACGACAACATTCTGAAGAGGAATTGAGAACTACTATGATGATCTGGACTTCAAA
AACATCATGGACTTTGTTCAGAAAAAGTTCAAGTGCTGTGGCGGGGAGGACTACCGAGATTG
GAGCAAGAATCAGTACCACGACTGCAGTGCCCCTGGACCCCTGGCCTGTGGGGTGCCCTACA
CCTGCTGCATCAGGAACACGACAGAAGTTGTCAACACCATGTGTGGCTACAAAACCTATCGAC
AAGGAGCGTTTCAGTGTGCAGGATGTCATCTACGTGCGGGGCTGCACCAACGCCGTGATCAT
CTGGTTCATGGACAACCTACACCATCATGGCGTGCATCCTCCTGGGCATCCTGCTTCCCCAGT
TCCTGGGGGTGCTGCTGACGCTGCTGTACATCACCCGGGTGGAGGACATCATCATGGAGCAC
TCTGTCACTGATGGGCTCCTGGGGCCCCGGTGCCAAGCCCAGCGTGGAGGCGGCAGGCACGGG
ATGCTGCTTGTGCTACCCCAATTAGGGGCCAGCCTGCCATGGCAGCTCCAACAAGGACCGTC
TGGGATAGCACCTCTCAGTCAACATCGTGGGGCTGGACAGGGCTGCGGCCCCCTCTGCCACA
CTCAGTACTGACCAAAGCCAGGGCTGTGTGTGCCTGTGTGTAGGTCCCACGGCCTCTGCCTC
CCCAGGGAGCAGAGCCTGGGCCTCCCCTAAGAGGCTTTCCCCGAGGCAGCTCTGGAATCTGT
GCCACCTGGGGCCTGGGGAACAAGGCCCTCCTTTCTCCAGGCCTGGGCTACAGGGGAGGGA
GAGCCTGAGGCTCTGCTCAGGGCCCATTTTCATCTCTGGCAGTGCTTGGCGGTGGTATTCAA
GGCAGTTTTGTAGCACCTGTAATTGGGGAGAGGGAGTGTGCCCTCGGGGCAGGAGGGAAGG
GCATCTGGGGAAGGGCAGGAGGGAAGAGCTGTCCATGCAGCCACGCCCATGGCCAGGTTGGC
CTCTTCTCAGCCTCCCAGGTGCCTTGAGCCCTCTTGCAAGGGCGGCTGCTTCCTTGAGCCTA
GTTTTTTTTTACGTGATTTTTGTAAACATTCATTTTTTTGTACAGATAACAGGAGTTTCTGAC
TAATCAAAGCTGGTATTTCCCCGCATGTCTTATTCTTGCCCTTCCCCCAACCAGTTTGTAA
TCAAACAATAAAAACATGTTTTGTTTTGTTTTTAAAAAAA

FIGURE 70

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64863

><subunit 1 of 1, 294 aa, 1 stop

><MW: 33211, pI: 5.35, NX(S/T): 3

MPRGDSEQVRYCARFSYLWLKFSLLIYSTVFWLIGALVLSVGIYAEVERQKYKTLES AFLAP
AIILILLGVVMFMVSFIGVLASLRDNLVLLQAFMYILGICLIMELIGGVVALTFRNQ TIDFL
NDNIRRGIE NYDDLD FKNIMDFVQKKFKCCGGEDYRDWSKNQYHDCSAPGPLACGV PYTCC
IRNTTEVVNTMCGYKTIDKERFSVQDVIYVRGCTNAVI IWFMDNYTIMACILLGILLPQFLG
VLLTLLYITRVEDIIMEHSVTDG LLGPGAKPSVEAAGTGCCLCYPN

Signal peptide:

amino acids 1-44

Transmembrane domains:

amino acids 22-42, 57-85, 93-116, 230-257

FIGURE 71

GAGGAGCGGGCCGAGGACTCCAGCGTGCCCAGGTCTGGCATCCTGCACTTGCTGCCCTCTGA
CACCTGGGAAGATGGCCGGCCCGTGGACCTTCACCCTTCTCTGTGGTTTGCTGGCAGCCACC
TTGATCCAAGCCACCCTCAGTCCCAGTGCAGTTCTCATCCTCGGCCCAAAGTCATCAAAGA
AAAGCTGACACAGGAGCTGAAGGACCACAACGCCACCAGCATCCTGCAGCAGCTGCCGCTGC
TCAGTGCCATGCGGGAAAAGCCAGCCGGAGGCATCCCTGTGCTGGGCAGCCTGGTGAACACC
GTCCTGAAGCACATCATCTGGCTGAAGGTCATCACAGCTAACATCCTCCAGCTGCAGGTGAA
GCCCTCGGCCAATGACCAGGAGCTGCTAGTCAAGATCCCCCTGGACATGGTGGCTGGATTCA
ACACGCCCCCTGGTCAAGACCATCGTGGAGTTCCACATGACGACTGAGGCCCAAGCCACCATC
CGCATGGACACCAGTGCAAGTGGCCCCACCCGCTGGTCCTCAGTGACTGTGCCACCAGCCA
TGGGAGCCTGCGCATCCAAGTGTGTATAAGCTCTCCTTCCTGGTGAACGCCTTAGCTAAGC
AGGTCATGAACCTCCTAGTGCCATCCCTGCCCAATCTAGTGAAAAACCAGCTGTGTCCCGTG
ATCGAGGCTTCCTTCAATGGCATGTATGCAGACCTCCTGCAGCTGGTGAAGGTGCCCATTTTC
CCTCAGCATTGACCGTCTGGAGTTTGACCTTCTGTATCCTGCCATCAAGGGTGACACCATTTC
AGCTCTACCTGGGGGCCAAGTTGTTGGACTCACAGGGAAAGGTGACCAAGTGGTTCAATAAC
TCTGCAGCTTCCCTGACAATGCCACCCTGGACAACATCCCGTTCAGCCTCATCGTGAGTCA
GGACGTGGTGAAAGCTGCAGTGGCTGCTGTGCTCTCTCCAGAAGAATTCATGGTCCTGTTGG
ACTCTGTGCTTCCTGAGAGTGCCCATCGGCTGAAGTCAAGCATCGGGCTGATCAATGAAAAG
GCTGCAGATAAGCTGGGATCTACCCAGATCGTGAAGATCCTAACTCAGGACACTCCCGAGTT
TTTTATAGACCAAGGCCATGCCAAGGTGGCCCAACTGATCGTGCTGGAAGTGTTTCCCTCCA
GTGAAGCCCTCCGCCCTTTGTTCAACCCTGGGCATCGAAGCCAGCTCGGAAGCTCAGTTTTAC
ACCAAAGGTGACCAACTTATACTCAACTTGAATAACATCAGCTCTGATCGGATCCAGCTGAT
GAACTCTGGGATTGGCTGGTTCCAACCTGATGTTCTGAAAAACATCATCACTGAGATCATCC
ACTCCATCCTGCTGCCGAACCAGAATGGCAAATTAAGATCTGGGGTCCCAGTGTCATTGGTG
AAGGCCTTGGGATTCGAGGCAGCTGAGTCCTCACTGACCAAGGATGCCCTTGTGCTTACTCC
AGCCTCCTTGTGGAAACCCAGCTCTCCTGTCTCCAGTGAAGACTTGGATGGCAGCCATCAG
GGAAGGCTGGGTCCCAGCTGGGAGTATGGGTGTGAGCTCTATAGACCATCCCTCTCTGCAAT
CAATAAACACTTGCCTGTGAAAAA

FIGURE 72

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64881

><subunit 1 of 1, 484 aa, 1 stop

><MW: 52468, pI: 7.14, NX(S/T): 3

MAGPWTFTLLCGLLAATLIQATLSPTAVLILGPKVIKEKLTQELKDHNATSILQQLPILLSAM
REKPAGGIPVLGSLVNTVLKHI IWLKVITANILQLQVKPSANDQELLVKIPLDMVAGFNTPL
VKTIVEFHMTTEAQATIRMDTSASGPTRLVLSDCATSHGSLRIQLLYKLSFLVNALAKQVMN
LLVPSLPNLVKNQLCPVIEASFNGMYADLLQLVKVPISLSIDRLEFDLLYPAIKGDTIQLYL
GAKLLDSQGKVTKWFNNSAASLTMPITLDNIPFSLIVSQDVVKAABAVALSPEEFMVLLDSVL
PESAHRLKSSIGLINEKAADKLGSTQIVKILTQDTPEFFIDQGHAKVAQLIVLEVFPSSSEAL
RPLFTLGIEASSEAQFYTKGDQLILNLNNISSDRIQLMNSGIGWFQPDVLKNIITEIIHSIL
LPNQNGKLRSGVPVSLVKALGFEEAESSLTKDALVLTPASLWKPSSPVSQ

Important features of the protein:

Signal peptide:

amino acids 1-21

N-glycosylation sites.

amino acids 48-51, 264-267, 401-404

Glycosaminoglycan attachment site.

amino acids 412-415

LBP / BPI / CETP family proteins.

amino acids 407-457

FIGURE 73

GAGCGAACATGGCAGCGCGTTGGCGGTTTTGGTGTGTCTCTGTGACCATGGTGGTGGCGCTG
CTCATCGTTTGGCGACGTTCCCTCAGCCTCTGCCCAAAGAAAGAAGGAGATGGTGTATCTGA
AAAGGTTAGTCAGCTGATGGAATGGACTAACAAAAGACCTGTAATAAGAATGAATGGAGACA
AGTTCCGTCGCCTTGTGAAAGCCCCACCGAGAAATTAATCCGTTATCGTCATGTTCACTGCT
CTCCAACCTGCATAGACAGTGTGTCGTTTGCAAGCAAGCTGATGAAGAATTCAGATCCTGGC
AAACTCCTGGCGATACTCCAGTGCATTCACCAACAGGATATTTTTTGGCATGGTGGATTTTG
ATGAAGGCTCTGATGTATTTTCAGATGCTAAACATGAATTCAGCTCCAACTTTCATCAACTTT
CCTGCAAAAGGGAAACCCAAACGGGGTGATACATATGAGTTACAGGTGCGGGGTTTTTCAGC
TGAGCAGATTGCCCGGTGGATCGCCGACAGAACTGATGTCAATATTAGAGTGATTAGACCCC
CAAATTATGCTGGTCCCCTTATGTTGGGATTGCTTTTGGCTGTTATTGGTGGACTTGTGTAT
CTTCGAAGAAGTAATATGGAATTTCTCTTTAATAAACTGGATGGGCTTTTGCAGCTTTGTG
TTTTGTGCTTGCTATGACATCTGGTCAAATGTGGAACCATATAAGAGGACCACCATATGCCC
ATAAGAATCCCCACACGGGACATGTGAATTATATCCATGGAAGCAGTCAAGCCCAGTTTGTA
GCTGAAACACACATTGTTCTTCTGTTTAATGGTGGAGTTACCTTAGGAATGGTGGCTTTTATG
TGAAGCTGCTACCTCTGACATGGATATTGGAAGCGAAAGATAATGTGTGTGGCTGGTATTG
GACTTGTTGTATTATTCTTCAGTTGGATGCTCTCTATTTTTTAGATCTAAATATCATGGCTAC
CCATACAGCTTTCTGATGAGTTAAAAAGGTCCCAGAGATATATAGACACTGGAGTACTGGAA
ATTGAAAAACGAAAATCGTGTGTGTTTGAAAAGAAGAATGCAACTTGTATATTTTGTATTAC
CTCTTTTTTTCAAGTGATTTAAATAGTTAATCATTTAACCAAAGAAGATGTGTAGTGCCTTA
ACAAGCAATCCTCTGTCAAAATCTGAGGTATTTGAAAATAATTATCCTCTTAACCTTCTCTT
CCCAGTGAACCTTTATGGAACATTTAATTTAGTACAATTAAGTATATTATAAAAATTGTAAAA
CTACTACTTTGTTTTAGTTAGAACAAAGCTCAAACTACTTTAGTTAACTTGGTCATCTGAT
TTTATATTGCCTTATCCAAAGATGGGGAAAGTAAGTCCTGACCAGGTGTTCCACATATGCC
TGTTACAGATAACTACATTAGGAATTCATTCTTAGCTTCTTCATCTTTGTGTGGATGTGTAT
ACTTTACGCATCTTTCCTTTTGAGTAGAGAAATTATGTGTGTGTCATGTGGTCTTCTGAAAATG
GAACACCATTCTTCAGAGCACACGTCTAGCCCTCAGCAAGACAGTTGTTTCTCCTCCTCCTT
GCATATTTCTACTGCGCTCCAGCCTGAGTGATAGAGTGAGACTCTGTCTCAAAAAAAGTA
TCTCTAAATACAGGATTATAATTTCTGCTTGAGTATGGTGTAACTACCTTGTATTTAGAAA
GATTTTCAGATTCAATCCATCTCCTTAGTTTTCTTTTAAGGTGACCCATCTGTGATAAAAATA
TAGCTTAGTGCTAAAATCAGTGTAACCTTATACATGGCCTAAAATGTTTCTACAAATTAGAGT
TTGTCACTTATTCCATTTGTACCTAAGAGAAAAATAGGCTCAGTTAGAAAAGGACTCCCTGG
CCAGGCGCAGTGACTTACGCCTGTAATCTCAGCACTTTGGGAGGCCAAGGCAGGCAGATCAC
GAGGTCAGGAGTTCGAGACCATCCTGGCCAACATGGTGAAACCCCGTCTCTACTAAAAATAT
AAAAATTAGCTGGGTGTGGTGGCAGGAGCCTGTAATCCCAGCTACACAGGAGGCTGAGGCAC
GAGAATCACTTGAACCTCAGGAGATGGAGGTTTCAGTGAGCCGAGATCACGCCACTGCACTCC
AGCCTGGCAACAGAGCGAGACTCCATCTCAAAAAAAAAAAAAA

FIGURE 74

MAARWRFWCVSVTMVVALLI VCDVPSASAQRKKEMVLSEKVSQ LMEWTNKR PVIRMNGDKFR
RLVKAPPRNYSVIVMFTALQLHRQCVVCKQADEEFQILANSWRYSSAFTNRIF FAMVDFDEG
SDVFQMLNMNSAPTFINFPAKGKPKRGDTYELQVRGFSAEQIARWIADRTDVNIRVIRPPNY
AGPLMLGLLLAVIGGLVYLRRSNMEFLFNKTGWAFALCFVLAMTSGQMWNHIRGPPYAHKN
PHTGHVNYIHGSSQAQFVAETHIVLLENGGVTLGMVLLCEAATSDMDIGKRKIMCVAGIGLV
VLFFSWMLSIFRSKYHGYPSFLMS

Signal peptide:

amino acids 1-29

Transmembrane domains:

amino acids 183-205, 217-237, 217-287, 301-321

FIGURE 75

AAGCAACCAAACCTGCAAGCTTTGGGAGTTGTTGCTGTCCCTGCCCTGCTCTGCTAGGGAGA
GAACGCCAGAGGGAGGCGGCTGGCCCGGCGGCAGGCTCTCAGAACCGCTACCGGCGGATGCTA
CTGCTGTGGGTGTGCGGTGGTTCGCAGCCTTGGCGCTGGCGGTACTGGCCCCCGGAGCAGGGGA
GCAGAGGCGGAGAGCAGCCAAAGCGCCCAATGTGGTGCTGGTCGTGAGCGACTCCTTCGATG
GAAGGTTAACATTTTCATCCAGGAAGTCAGGTAGTGAAACTTCCTTTTATCAACTTTATGAAG
ACACGTGGGACTTCCTTTCTGAATGCCTACACAACTCTCCAATTTGTTGCCCATCACGCGC
AGCAATGTGGAGTGGCCTCTTCACTCACTTAACAGAATCTTGGAATAATTTTAAGGGTCTAG
ATCCAAATTATACAACATGGATGGATGTCATGGAGAGGCATGGCTACCGAACACAGAAATTT
GGGAACTGGACTATACTTCAGGACATCACTCCATTAGTAATCGTGTGGAAGCGTGGACAAG
AGATGTTGCTTTCTTACTCAGACAAGAAGGCAGGCCCATGGTTAATCTTATCCGTAACAGGA
CTAAAGTCAGAGTGATGGAAAGGGATTGGCAGAATACAGACAAAGCAGTAAACTGGTTAAGA
AAGGAAGCAATTAATTACACTGAACCATTTGTTATTTTACTTGGGATTAAATTTACCACACCC
TTACCCTTCACCATCTTCTGGAGAAAATTTTGGATCTTCAACATTTACACATCTCTTTATT
GGCTTGAAAAAGTGTCTCATGATGCCATCAAATCCCAAAGTGGTCACCTTTGTCAGAAATG
CACCCTGTAGATTATTACTCTTCTTATACAAAAAACTGCACTGGAAGATTTACAÀAAAAAGA
AATTAAGAATATTAGAGCATTTTATTATGCTATGTGTGCTGAGACAGATGCCATGCTTGGTG
AAATTATTTTGGCCCTTCATCAATTAGATCTTCTTCAGAAAACCTATTGTCATATACTCCTCA
GACCATGGAGAGCTGGCCATGGAACATCGACAGTTTTTATAAAATGAGCATGTACGAGGCTAG
TGCACATGTTCCGCTTTTGATGATGGGACCAGGAATTAAAGCCGGCCTACAAGTATCAAATG
TGGTTTCTCTTGTGGATATTTACCCTACCATGCTTGATATTGCTGGAATTCCTCTGCCTCAG
AACCTGAGTGGATACTCTTTGTTGCCGTTATCATCAGAAACATTTAAGAATGAACATAAAGT
CAAAAACCTGCATCCACCCTGGATTCTGAGTGAATTCCATGGATGTAATGTGAATGCCTCCA
CCTACATGCTTCGAACTAACCCTGGAAATATATAGCCTATTCCGATGGTGCATCAATATTG
CCTCAACTCTTTGATCTTTCTCGGATCCAGATGAATTAACAAATGTTGCTGTAAAATTTCC
AGAAATTACTTATTCTTTGGATCAGAAGCTTCATTCCATTATAAACTACCCTAAAGTTTCTG
CTTCTGTCCACCAGTATAATAAAGAGCAGTTTATCAAGTGGAAACAAAGTATAGGACAGAAT
TATTCAAACGTTATAGCAAATCTTAGGTGGCACCAAGACTGGCAGAAGGAACCAAGGAAGTA
TGAAAATGCAATTGATCAGTGGCTTAAAACCCATATGAATCCAAGAGCAGTTTGAACAAAAA
GTTTAAAAATAGTGTTCTAGAGATACATATAAATATATTACAAGATCATAATTATGTATTTT
AAATGAAACAGTTTTTAATAATTACCAAGTTTTTGGCCGGGCACAGTGGCTCACACCTGTAATC
CCAGGACTTTGGGAGGCTGAGGAAAGCAGATCACAAGGTCAAGAGATTGAGACCATCCTGGC
CAACATGGTGAAACCCTGTCTCTACTAAAAATACAAAAATTAGCTGGGCGCGGTGGTGACA
CCTATAGTCTCAGCTACTCAGAGGCTGAGGCAGGAGGATCGCTTGAACCCGGGAGGCAGCAG
TTGCAGTGAGCTGAGATTGCGCCACTGTACTCCAGCCTGGCAACAGAGTGAGACTGTGTGCG
AAAAAAATAAAAAATAAATAATAATTACCAATTTTTTCATTATTTTGTAAGAATGTAGTG
TATTTTAAGATAAAATGCCAATGATTATAAAATCACATATTTTCAAAAATGGTTATTATTTA
GGCCTTTGTACAATTTCTAACAATTTAGTGGAAGTATCAAAGGATTGAAGCAAATACTGTA
ACAGTTATGTTCCCTTTAAATAATAGAGAATATAAAATATTGTAATAATATGTATCATAAAAT
AGTTGTATGTGAGCATTTGATGGTGAAAAAÀAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAA

FIGURE 76

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64885

<subunit 1 of 1, 536 aa, 1 stop

<MW: 61450, pI: 9.17, NX(S/T): 7

MLLLWVSVVAALALAVLAPGAGEQRRRAAKAPNVVLVVSDSFDGRLTFHPGSQVVKLPFINF
MKTRGTSFLNAYTNSPICCPRAAMWSGLFTHLTESWNNFKGLDPNYTTWMDVMERHGYRTQ
KFGKLDYTSGHHSISNRVEAWTRDVAFLLRQEGRPMVNLIRNRTKVRVMERDWQNTDKAVNW
LRKEAINYTEPFVIYLGLNLPHYPSPSSGENFGSSTFHTSLYWLEKVSHDAIKIPKWSPLS
EMHPVDYYSSYTKNCTGRFTKKEIKNIRAFYYAMCAETDAMLGEIILALHQLDLLQKTIVIIY
SSDHGELAMEHRQFYKMSMYEASAHVPLLMMGPGIKAGLQVSNVSLVDIYPTMLDIAGIPL
PQNLSGYSLPLSSETFKNEHKVKNLHPPWILSEFHGCNVNASTYMLRTNHWKYIAYSDGAS
ILPQLFDLSSDPDELTNVAVKFPEITYSLDQKLHSIINYPKVSASVHQYNKEQFIKWKQSIG
QNYSNVIANLRWHQDWQKEPRKYENAIQWLKTHMNPRAV

Important features:

Signal peptide:

amino acids 1-15

N-glycosylation sites.

amino acids 108-111, 166-169, 193-196, 262-265, 375-378, 413-416,
498-501

Sulfatases proteins:

amino acids 286-315, 359-369, 78-97

FIGURE 77

GAGAGAAGTCAGCCTGGCAGAGAGACTCTGAAATGAGGGATTAGAGGTGTTCAAGGAGCAAG
AGCTTCAGCCTGAAGACAAGGGAGCAGTCCCTGAAGACGCTTCTACTGAGAGGTCTGCCATG
GCCTCTCTTGGCCTCCAACCTTGTGGGCTACATCCTAGGCCTTCTGGGGCTTTTGGGCACACT
GGTTGCCATGCTGCTCCCCAGCTGGAAAACAAGTTCTTATGTCGGTGCCAGCATTGTGACAG
CAGTTGGCTTCTCCAAGGGCCTCTGGATGGAATGTGCCACACACAGCACAGGCATCACCCAG
TGTGACATCTATAGCACCCCTTCTGGGCCTGCCCCTGACATCCAGGCTGCCCAGGCCATGAT
GGTGACATCCAGTGCAATCTCCTCCCTGGCCTGCATTATCTCTGTGGTGGGCATGAGATGCA
CAGTCTTCTGCCAGGAATCCCGAGCCAAAGACAGAGTGGCGGTAGCAGGTGGAGTCTTTTTC
ATCCTTGGAGGCCTCCTGGGATTCAATTCCTGTTGCCTGGAATCTTCATGGGATCCTACGGGA
CTTCTACTCACCACTGGTGCCTGACAGCATGAAATTTGAGATTGGAGAGGCTCTTTACTTGG
GCATTATTTCTTCCCTGTTCTCCCTGATAGCTGGAATCATCCTCTGCTTTTCCTGCTCATCC
CAGAGAAATCGCTCCAACCTACTACGATGCCTACCAAGCCCAACCTCTTGCCACAAGGAGCTC
TCCAAGGCCTGGTCAACCTCCCAAAGTCAAGAGTGAGTTCAATTCCTACAGCCTGACAGGGT
ATGTGTGAAGAACCAGGGGCCAGAGCTGGGGGGTGGCTGGGTCTGTGAAAAACAGTGGACAG
CACCCCGAGGGCCACAGGTGAGGGACACTACCACTGGATCGTGTGAGAAGGTGCTGCTGAGG
ATAGACTGACTTTGGCCATTGGATTGAGCAAAGGCAGAAATGGGGGCTAGTGTAACAGCATG
CAGGTTGAATTGCCAAGGATGCTCGCCATGCCAGCCTTTCTGTTTTCTCACCTTGCTGCTC
CCCTGCCCTAAGTCCCCAACCTCAACTTGAAACCCCATTCCTTAAGCCAGGACTCAGAGG
ATCCCTTTGCCCTCTGGTTTACCTGGGACTCCATCCCCAAACCCACTAATCACATCCCCTG
ACTGACCCTCTGTGATCAAAGACCCTCTCTCTGGCTGAGGTTGGCTCTTAGCTCATTGCTGG
GGATGGGAAGGAGAAGCAGTGGCTTTTGTGGGCATTGCTCTAACCTACTTCTCAAGCTTCCC
TCCAAAGAACTGATTGGCCCTGGAACCTCCATCCCCTCTTGTTATGACTCCACAGTGTCC
AGACTAATTTGTGCATGAACTGAAATAAAACCATCCTACGGTATCCAGGGAACAGAAAGCAG
GATGCAGGATGGGAGGACAGGAAGGCAGCCTGGGACATTTAAAAAATA

FIGURE 78

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64886

><subunit 1 of 1, 230 aa, 1 stop

><MW: 24549, pI: 8.56, NX(S/T): 1

MASLGLQLVG YILG LLG LLG TLVAMLLPSWKTSSYVGASIVTAVGFSKGLWMECATHSTGIT
QCDIYSTLLGLPADIQAAQAMMVTSSAIISSLACIISVVGMRCTVFCQESRAKDRVAVAGGVF
FILG LLGFIPVAWN LHGILRDFYSPLVPDSMKFEIGEALYLGIISSLFSLIAGIILCFSCS
SQRNRSNYYDAYQAQPLATRSSPRPGQPPKVKSEFNSYSLTGYV

Important features of the protein:

Signal peptide:

amino acids 1-24

Transmembrane domains:

amino acids 82-102, 117-140, 163-182

N-glycosylation site.

amino acids 190-193

PMP-22 / EMP / MP20 family proteins.

amino acids 46-59

FIGURE 79

GCAC TGCTGCTGTCCCATCAGCTGCTCTGAAGCTCCATGGTGCC CAGAATCTTCGCTCCTGC
TTATGTGTCAGTCTGTCTCCTCCTCTTGTTGTCCAAGGGAAGTCATCGCTCCCGCTGGCTCAG
AACCATGGCTGTGCCAGCCGGCACCCAGGTGTGGAGACAAGATCTACAACCCCTTGGAGCAG
TGCTGTTACAATGACGCCATCGTGTCCCTGAGCGAGACCCGCCAATGTGGTCCCCCCTGCAC
CTTCTGGCCCTGCTTTGAGCTCTGCTGTCTTGATTCCTTTGGCCTCACAAACGATTTTGTTG
TGAAGCTGAAGGTTCAAGGTGTGAATTCCCAGTGCCACTCATCTCCCATCTCCAGTAAATGT
GAAAGCAGAAGACGTTTTCCCTGAGAGAAGACATAGAAAGAAAATCAACTTTCAC TAAGGCATC
TCAGAAACATAGGCTAAGGTAATATGTGTACCAGTAGAGAAGCCTGAGGAATTTACAAAATG
ATGCAGCTCCAAGCCATTGTATGGCCCATGTGGGAGACTGATGGGACATGGAGAATGACAGT
AGATTATCAGGAAATAAATAAAGTGGTTTTTCCAATGTACACACCTGTAAAA

FIGURE 80

MVPRI FAPAYVSVCLLLCPREVIAPAGSEPWLCQPAPRCGDKIYNPLEQCCYNDAIVSLSE
TRQCGPPCTFWPCFELCCLDSFGLTNDFFVVKLVQGVNSQCHSSPISSKCESRRRFP

Signal peptide:
amino acids 1-25

FIGURE 81

CTCCACTGCAACCACCCAGAGCCATGGCTCCCCGAGGCTGCATCGTAGCTGTCTTTGCCATT
TTCTGCATCTCCAGGCTCCTCTGCTCACACGGAGCCCCAGTGGCCCCCATGACTCCTTACCT
GATGCTGTGCCAGCCACACAAGAGATGTGGGGACAAGTTCTACGACCCCCCTGCAGCACTGTT
GCTATGATGATGCCGTCGTGCCCTTGGCCAGGACCCAGACGTGTGGAACTGCACCTTCAGA
GTCTGCTTTGAGCAGTGCTGCCCCCTGGACCTTCATGGTGAAGCTGATAAACAGAACTGCGA
CTCAGCCCCGACCTCGGATGACAGGCTTTGTTCGCAGTGTCAGCTTAATGGAACATCAGGGGAA
CGATGACTCCTGGATTCTCCTTCCTGGGTGGGCCTGGAGAAAGAGGCTGGTGTTACCTGAGA
TCTGGGATGCTGAGTGGCTGTTTGGGGGCCAGAGAAACACACACTCAACTGCCCACCTTCATT
CTGTGACCTGTCTGAGGCCACCCTGCAGCTGCCCTGAGGAGGCCACAGGTCCCCTTCTAG
AATTCTGGACAGCATGAGATGCGTGTGCTGATGGGGGCCAGGGACTCTGAACCCTCCTGAT
GACCCTATGGCCAACATCAACCCGGCACCACCCCAAGGCTGGCTGGGGAACCCTTCACCCT
TCTGTGAGATTTTCCATCATCTCAAGTTCTCTTCTATCCAGGAGCAAAGCACAGGATCATAA
TAAATTTATGTACTTTATAAATGAAAA

FIGURE 82

MAPRGCIVAVFAIFCISRLLC SHGAPVAPMTPYLMLCQPHKRCGDKFYDPLQHCCYDDAVVP
LARTQTCGNCTFRVC FEQCCPWTFMVKLINQNCD SARTSDDR LCRSVS

Signal peptide:
amino acids 1-24

GGGGGCGGGTGCCTGGAGCACGGCGCTGGGGGCCGCCCGCAGCGCTCACTCGCTCGCACTCAG
TCGCGGGAGGCTTCCCCGCGCCGGCCGCGTCCCGCCCGCTCCCCGGCACCAGAAGTTCCTCT
GCGCGTCCGACGGCGACATGGGCGTCCCCACGGCCCTGGAGGCCGGCAGCTGGCGCTGGGGA
TCCCTGCTCTTCGCTCTCTTCCCTGGCTGCGTCCCTAGGTCCGGTGGCAGCCTTCAAGGTCGC
CACGCCGTATTCCCTGTATGTCTGTCCCGAGGGGGCAGAACGTCAACCTCACCTGCAGGCTCT
TGGGCCCTGTGGACAAAGGGCACGATGTGACCTTCTACAAGACGTGGTACCGCAGCTCGAGG
GGCGAGGTGCAGACCTGCTCAGAGCGCCGGCCCATCCGCAACCTCACGTTCCAGGACCTTCA
CCTGCACCATGGAGGCCACCAGGCTGCCAACACCAGCCACGACCTGGCTCAGCGCCACGGGC
TGGAGTCGGCCTCCGACCACCATGGCAACTTCTCCATCACCATGCGCAACCTGACCCTGCTG
GATAGCGGCCTCTACTGCTGCCTGGTGGTGGAGATCAGGCACCACCACCTCGGAGCACAGGGT
CCATGGTGCCATGGAGCTGCAGGTGCAGACAGGCAAAGATGCACCATCCAACCTGTGTGGTGT
ACCCATCCTCCTCCCAGGATAGTGAAAACATCACGGCTGCAGCCCTGGCTACGGGTGCCTGC
ATCGTAGGAATCCTCTGCCTCCCCCTCATCCTGCTCCTGGTCTACAAGCAAAGGCAGGCAGC
CTCCAACCGCCGTGCCCAGGAGCTGGTGC GGATGGACAGCAACATTCAAGGGATTGAAAACC
CCGGCTTTGAAGCCTCACCACTGCCCAGGGGATACCCGAGGCCAAAGTCAGGCACCCCTG
TCCTATGTGGCCCAGCGGCAGCCTTCTGAGTCTGGGCGGCATCTGCTTTTCGGAGCCCAGCAC
CCCCCTGTCTCCTCCAGGCCCCGGAGACGTCTTCTTCCCATCCCTGGACCCTGTCCCTGACT
CTCCAAACTTTGAGGTCATCTAGCCCAGCTGGGGGACAGTGGGCTGTTGTGGCTGGGTCTGG
GGCAGGTGCATTTGAGCCAGGGCTGGCTCTGTGAGTGGCCTCCTTGGCCTCGGCCCTGGTTC
CCTCCCTCCTGCTCTGGGCTCAGATACTGTGACATCCCAGAAGCCCAGCCCTCAACCCCTC
TGGATGCTACATGGGGATGCTGGACGGCTCAGCCCTGTTCCAAGGATTTTGGGGTGCTGAG
ATTCTCCCCTAGAGACCTGAAATTCACCAGCTACAGATGCCAAATGACTTACATCTTAAGAA
GTCTCAGAACGTCCAGCCCTTCAGCAGCTCTCGTTCTGAGACATGAGCCTTGGGATGTGGCA
GCATCAGTGGGACAAGATGGACACTGGGCCACCCTCCCAGGCACCAGACACAGGGCACGGTG
GAGAGACTTCTCCCCCGTGGCCGCCCTTGGCTCCCCCGTTTTGCCCGAGGCTGCTCTTCTGTC
AGACTTCCTCTTTGTACCACAGTGGCTCTGGGGCCAGGCCTGCCTGCCCACTGGCCATCGCC
ACCTTCCCCAGCTGCCTCCTACCAGCAGTTTCTCTGAAGATCTGTCAACAGGTTAAGTCAAT
CTGGGGCTTCCACTGCCTGCATTCCAGTCCCCAGAGCTTGGTGGTCCCGAAACGGGAAGTAC
ATATTGGGGCATGGTGGCCTCCGTGAGCAAATGGTGTCTTGGGCAATCTGAGGCCAGGACAG
ATGTTGCCCCACCCACTGGAGATGGTGTCTGAGGGAGGTGGGTGGGGCCTTCTGGGAAGGTGA
GTGGAGAGGGGCACCTGCCCCCGCCCTCCCCATCCCTACTCCCCTGCTCAGCGCGGGCC
ATTGCAAGGGTGCCACACAATGTCTTGTCACCCCTGGGACACTTCTGAGTATGAAGCGGGAT
GCTATTAAAAACTACATGGGGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGA

FIGURE 84

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64897

><subunit 1 of 1, 311 aa, 1 stop

><MW: 33908, pI: 6.87, NX(S/T): 6

MGVPTALEAGSWRWGSLLFALFLAASLGPVAAFQVATPYSLYVCPEGQNVTLTCRLLGPVVK
GHDVTFYKTWYRSSRGEVQTCSERRPIRNLTFQDLHLHHGGHQAANTSHDLAQRHGLESASD
HHGNFSITMRNLTLDDSGLYCCLVVEIRHHHSEHRVHGAMELQVQTGKDAPSNCVVYPSSSQ
DSENITAAALATGACIVGILCLPLILLLVYKQRQAASNRRAQELVRMDSNIQGIENPGFEAS
PPAQGIPEAKVRHPLSYVAQRQPSESGRHLLSEPSTPLSPPGPGDVFFPSLDPVPDSPNFEVI

Signal peptide:

amino acids 1-28

Transmembrane domain:

amino acids 190-216

FIGURE 85

CCCACGCGTCCGCGCCTCTCCCTTCTGCTGGACCTTCCTTCGTCTCTCCATCTCTCCCTCCT
TTCCCCGCGTTCTCTTTCCACCTTTCTCTTCTTCCCACCTTAGACCTCCCTTCCTGCCCTCC
TTTCCTGCCCACCGCTGCTTCCTGGCCCTTCTCCGACCCCGCTCTAGCAGCAGACCTCCTGG
GGTCTGTGGGTTGATCTGTGGCCCCCTGTGCCTCCGTGTCCTTTTCGTCTCCCTTCCTCCCGA
CTCCGCTCCCGGACCAGCGGCCTGACCCTGGGGAAAGGATGGTTCCCGAGGTGAGGGTCCTC
TCCTCCTTGCTGGGACTCGCGCTGCTCTGGTTCCCCCTGGACTCCCACGCTCGAGCCCCGCC
AGACATGTTCTGCCTTTTCCATGGGAAGAGATACTCCCCCGGCGAGAGCTGGCACCCCTACT
TGGAGCCACAAGGCCTGATGTACTGCCTGCGCTGTACCTGCTCAGAGGGCGCCCATGTGAGT
TGTTACCGCCTCCACTGTCCGCCTGTCCACTGCCCCCAGCCTGTGACGGAGCCACAGCAATG
CTGTCCCAAGTGTGTGGAACCTCACACTCCCTCTGGACTCCGGGCCCCACCAAAGTCCTGCC
AGCACAACGGGACCATGTACCAACACGGAGAGATCTTCAGTGCCCATGAGCTGTTCCCTCC
CGCCTGCCCCAACCAGTGTGTCTCTGCAGCTGCACAGAGGGCCAGATCTACTGCGGCCTCAC
AACCTGCCCCGAACCAGGCTGCCCAGCACCCCTCCCCTGCCCAGACTCCTGCTGCCAAGCCT
GCAAAGATGAGGCAAGTGAGCAATCGGATGAAGAGGACAGTGTGCAGTCGCTCCATGGGGTG
AGACATCCTCAGGATCCATGTTCCAGTGATGCTGGGAGAAAGAGAGGCCCGGGCACCCAGC
CCCCACTGGCCTCAGCGCCCCTCTGAGCTTCATCCCTCGCCACTTCAGACCCAAGGGAGCAG
GCAGCACAACCTGTCAAGATCGTCCTGAAGGAGAAACATAAGAAAGCCTGTGTGCATGGCGGG
AAGACGTACTCCCACGGGGAGGTGTGGCACCCGGCCTTCCGTGCCTTCGGCCCCCTTGCCCTG
CATCCTATGCACCTGTGAGGATGGCCGCCAGGACTGCCAGCGTGTGACCTGTCCCACCGAGT
ACCCCTGCCGTACCCCCGAGAAAGTGGCTGGGAAGTGCTGCAAGATTTGCCCAGAGGACAAA
GCAGACCCTGGCCACAGTGAGATCAGTTCTACCAGGTGTCCCAAGGCACCGGGCCGGGTCTCT
CGTCCACACATCGGTATCCCCAAGCCCAGACAACCTGCGTCGCTTTGCCCTGGAACACGAGG
CCTCGGACTTGGTGGAGATCTACCTCTGGAAGCTGGTAAAAGATGAGGAACTGAGGCTCAG
AGAGGTGAAGTACCTGGCCCAAGGCCACACAGCCAGAATCTTCCACTTGACTCAGATCAAGA
AAGTCAGGAAGCAAGACTTCCAGAAAGAGGCACAGCACTTCCGACTGCTCGCTGGCCCCCAC
GAAGGTCACTGGAACGTCTTCCTAGCCCAGACCCTGGAGCTGAAGGTCACGGCCAGTCCAGA
CAAAGTGACCAAGACATAACAAAGACCTAAACAGTTGCAGATATGAGCTGTATAATTGTTGTT
ATTATATATTAATAAATAAGAAGTTGCATTACCCTCAAAAAAAAAAAAAAAAAAAAAA

FIGURE 86

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64902
><subunit 1 of 1, 451 aa, 1 stop
><MW: 49675, pI: 7.15, NX(S/T): 1
MVPEVRVLSSLLGLALLWFPLDSHARARPD MFCLFHGKRYSPGESWHPYLEPQGLMYCLRCT
CSEGAHVSCYRLHCPPVHCPQPVTEPQQCCPKCVEPHTPSGLRAPPKSCQHNGTMYQHGEIF
SAHELFPSRLPNQCVLCSCTEGQIYCGLTTCPEPGCPAPLPLPDSCCQACKDEASEQSDEED
SVQSLHGVRHPQDPCSSDAGRKRGP GTPAPTGLSAPLSFIPRHFRPKGAGSTTVKIVLKEKH
KKACVHGGKTYSHGEVWHPAFRAFGPLPCILCTCEDGRQDCQRVTCPT EYPCRHPKVAGKC
CKICPEDKADPGHSEISSTRCPKAPGRVLVHTSVSPSPDNLRRFALEHEASDLVEIYLWKL V
KDEETEAQRGEVPGPRPHSQNLPLDSDQESQEARLPERGTALPTARWP PRRSLEQLPSPDPG
AEGHGQSRQSDQDITKT
```

Signal peptide:

amino acids 1-25

FIGURE 87

CTAGCCTGCGCCAAGGGGTAGTGAGACCGCGCGGCAACAGCTTGCGGCTGCGGGGAGCTCCC
GTGGGCGCTCCGCTGGCTGTGCAGGCGGCCATGGATTCTTGCGGAAAATGCTGATCTCAGT
CGCAATGCTGGGCGCAGGGGCTGGCGTGGGCTACGCGCTCCTCGTTATCGTGACCCCGGGAG
AGCGGCGGAAGCAGGAAATGCTAAAGGAGATGCCACTGCAGGACCCAAGGAGCAGGGAGGAG
GCGGCCAGGACCCAGCAGCTATTGCTGGCCACTCTGCAGGAGGCAGCGACCACGCAGGAGAA
CGTGGCCTGGAGGAAGAACTGGATGGTTGGCGGCGAAGGCGGCGCCAGCGGGAGGTCACCGT
GAGACCGGACTTGCCTCCGTGGGCGCCGGACCTTGGCTTGGGCGCAGGAATCCGAGGCAGCC
TTTCTCCTTCGTGGGCCCAGCGGAGAGTCCGGACCGAGATACCATGCCAGGACTCTCCGGGG
TCCTGTGAGCTGCCGTCGGGTGAGCACGTTTCCCCCAAACCCTGGACTGACTGCTTTAAGGT
CCGCAAGGCGGGCCAGGGCCGAGACGCGAGTCGGATGTGGTGAACTGAAAGAACCAATAAAA
TCATGTTCTCCAA
AAAAAAAAAAAA

FIGURE 88

MDSLRKMLISVAMLGAGAGVGYALLVIVTPGERRKQEMLKEMPLQDPRSREEAARTQQLLLA
TLQEAATTQENVAWRKNWMVGEGGASGRSP

Signal peptide:
amino acids 1-18

FIGURE 89

CAGGAGAGAAGGCACCGCCCCACCCCGCCTCCAAAGCTAACCCCTCGGGCTTGAGGGGAAGA
GGCTGACTGTACGTTCCCTTCTACTCTGGCACCCTCTCCAGGCTGCCATGGGGCCCAGCACC
CCTCTCCTCATCTTGTTCCCTTTTGTTCATGGTCGGGACCCCTCCAAGGACAGCAGCACCACCT
TGTGGAGTACATGGAACGCCGACTAGCTGCTTTAGAGGAACGGCTGGCCCAGTGCCAGGACC
AGAGTAGTCGGCATGCTGCTGAGCTGCGGGACTTCAAGAACAAGATGCTGCCACTGCTGGAG
GTGGCAGAGAAGGAGCGGGAGGCACTCAGAACTGAGGCCGACACCATCTCCGGGAGAGTGGA
TCGTCTGGAGCGGGAGGTAGACTATCTGGAGACCCAGAACCCAGCTCTGCCCTGTGTAGAGT
TTGATGAGAAGGTGACTGGAGGCCCTGGGACCAAAGGCAAGGGAAGAAGGAATGAGAAGTAC
GATATGGTGACAGACTGTGGCTACACAATCTCTCAAGTGAGATCAATGAAGATTCTGAAGCG
ATTTGGTGGCCCAGCTGGTCTATGGACCAAGGATCCACTGGGGCAAACAGAGAAGATCTACG
TGTTAGATGGGACACAGAATGACACAGCCTTTGTCTTCCCAAGGCTGCGTGACTTCACCCTT
GCCATGGCTGCCCCGAAAGCTTCCCGAGTCCGGGTGCCCTTCCCCTGGGTAGGCACAGGGCA
GCTGGTATATGGTGGCTTTCTTTATTTTGCTCGGAGGCCTCCTGGAAGACCTGGTGGAGGTG
GTGAGATGGAGAACACTTTGCAGCTAATCAAATTCACCTGGCAAACCGAACAGTGGTGGAC
AGCTCAGTATTCCCAGCAGAGGGGCTGATCCCCCCTACGGCTTGACAGCAGACACCTACAT
CGACCTGGTAGCTGATGAGGAAGGTCTTTGGGCTGTCTATGCCACCCGGGAGGATGACAGGC
ACTTGTGTCTGGCCAAGTTAGATCCACAGACACTGGACACAGAGCAGCAGTGGGACACACCA
TGTCCCAGAGAGAATGCTGAGGCTGCCTTTGTTCATCTGTGGGACCCCTCTATGTCGTCTATAA
CACCCGTCCTGCCAGTCGGGCCCCGCATCCAGTGCTCCTTTGATGCCAGCGGCACCCTGACCC
CTGAACGGGCAGCACTCCCTTATTTTCCCCGCAGATATGGTGCCCATGCCAGCCTCCGCTAT
AACCCCCGAGAACGCCAGCTCTATGCCTGGGATGATGGCTACCAGATTGTCTATAAGCTGGA
GATGAGGAAGAAAGAGGAGGAGGTTTGAGGAGCTAGCCTTGTTTTTTGCATCTTTCTCACTC
CCATACATTTATATTATATCCCCACTAAATTTCTTGTTCCCTCATCTTCAAATGTGGGCCAG
TTGTGGCTCAAATCCTCTATATTTTGTAGCCAATGGCAATCAAATCTTTTCAGCTCCTTTGTT
TCATACGGAACTCCAGATCCTGAGTAATCCTTTTAGAGCCCGAAGAGTCAAAACCCTCAATG
TTCCCTCCTGCTCTCCTGCCCCATGTCAACAAATTTAGGCTAAGGATGCCCCAGACCCAGG
GCTCTAACCTTGTATGCGGGCAGGCCAGGGAGCAGGCAGCAGTGTTCTTCCCCTCAGAGTG
ACTTGGGGAGGGAGAAATAGGAGGAGACGTCCAGCTCTGTCCTCTCTTCTCACTCCTCCCT
TCAGTGTCTGAGGAACAGGACTTTCTCCACATTGTTTTGTATTGCAACATTTTGCATTAAA
AGGAAAATCCACAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 90

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64905

<subunit 1 of 1, 406 aa, 1 stop

<MW: 46038, pI: 6.50, NX(S/T): 2

MGPSTPLLILFLLSWGPLQGQQHHLVEYMERRLAALERLAQCQDQSSRHAAELRDFKNKM
LPLLEVAEKEREALRTEADTISGRVDRLEREVDYLETQNPALPCVEFDEKVTGGPGTKGKGR
RNEKYDMVTDCGYTISQVRSMKILKRFGGPAGLWTKDPLGQTEKIYVLDGTQNDTAFVFPRL
RDFTLAMAARKASRVRVPFPWVG TGQLVYGGFLYFARRPPGRP GGGGEMENTLQLIKFHLAN
RTVVDSSVFPAEGLIPPYGLTADTYIDLVADEEGLWAVYATREDDRHLCLAKLDPQTL DTEQ
QWDTPCPRENAEAAAFVICGTLYVVYNTRPASRARIQCSFDASGTLTPERAALPYFPRRYGAH
ASLRYNPRERQLYAWDDGYQIVYKLEMRKKEEEV

Important features:

Signal peptide:

amino acids 1-21

N-glycosylation sites.

amino acids 177-180, 248-251

FIGURE 91

GACAGCTGTGTCTCGATGGAGTAGACTCTCAGAACAGCGCAGTTTGCCCTCCGCTCACGCAG
AGCCTCTCCGTGGCTTCCGCACCTTGAGCATTAGGCCAGTTCTCCTCTTCTCTCTAATCCAT
CCGTCACCTCTCCTGTCATCCGTTTCCATGCCGTGAGGTCCATTACAGAACACATCCATGG
CTCTCATGCTCAGTTTGGTTCTGAGTCTCCTCAAGCTGGGATCAGGGCAGTGGCAGGTGTTT
GGGCCAGACAAGCCTGTCCAGGCCTTGGTGGGGGAGGACGCAGCATTCTCCTGTTTCTGTGTC
TCCTAAGACCAATGCAGAGGCCATGGAAGTGCGGTTCTTCAGGGGCCAGTTCTCTAGCGTGG
TCCACCTCTACAGGGACGGGAAGGACCAGCCATTTATGCAGATGCCACAGTATCAAGGCAGG
ACAAAACCTGGTGAAGGATTCTATTGCGGAGGGGCGCATCTCTCTGAGGCTGGAAAACATTAC
TGTGTTGGATGCTGGCCTCTATGGGTGCAGGATTAGTTCCCAGTCTTACTACCAGAAGGCCA
TCTGGGAGCTACAGGTGTCAGCACTGGGCTCAGTTCCTCTCATTTCATCACGGGATATGTT
GATAGAGACATCCAGCTACTCTGTCAGTCCTCGGGCTGGTTCCCCCGGGCCACAGCGAAGTG
GAAAGGTCCACAAGGACAGGATTTGTCCACAGACTCCAGGACAAACAGAGACATGCATGGCC
TGTTTGATGTGGAGATCTCTCTGACCGTCCAAGAGAACGCCGGGAGCATATCCTGTTCCATG
CGGCATGCTCATCTGAGCCGAGAGGTGGAATCCAGGGTACAGATAGGAGATACCTTTTTTCGA
GCCTATATCGTGGCACCTGGCTACCAAAGTACTGGGAATACTCTGCTGTGGCCTATTTTTTG
GCATTGTTGGACTGAAGATTTTCTTCTCCAAATTCAGTGGAATAATCCAGGCGGAACCTGGAC
TGGAGAAGAAAGCACGGACAGGCAGAATTGAGAGACGCCCCGGAACACGCAGTGGAGGTGAC
TCTGGATCCAGAGACGGCTCACCCGAAGCTCTGCGTTTCTGATCTGAAAACCTGTAACCCATA
GAAAAGCTCCCCAGGAGGTGCCTCACTCTGAGAAGAGATTTACAAGGAAGAGTGTGGTGGCT
TCTCAGAGTTTCCAAGCAGGGAAACATTAAGTGGGAGGTGGACGGAGGACACAATAAAAGGTG
GCGCGTGGGAGTGTGCCGGGATGATGTGGACAGGAGGAAGGAGTACGTGACTTTGTCTCCCG
ATCATGGGTACTGGGTCTCAGACTGAATGGAGAACATTTGTATTTACATTAAATCCCCGT
TTTATCAGCGTCTTCCCCAGGACCCACCTACAAAATAGGGGTCTTCCTGGACTATGAGTG
TGGGACCATCTCCTTCTTCAACATAAATGACCAGTCCCTTATTTATACCCTGACATGTCCGT
TTGAAGGCTTATTGAGGCCCTACATTGAGTATCCGTCTTATAATGAGCAAAATGGAACCTCCC
ATAGTCATCTGCCCAGTCACCCAGGAATCAGAGAAAGAGGCCTCTTGGCAAAGGGCCTCTGC
AATCCCAGAGACAAGCAACAGTGAGTCCTCCTCACAGGCAACCACGCCCTTCCTCCCCAGGG
GTGAAATGTAGGATGAATCACATCCCACATTCTTCTTTAGGGATATTAAGGTCTCTCTCCA
GATCCAAAGTCCCGCAGCAGCCGGCCAAGGTGGCTTCCAGATGAAGGGGGACTGGCCTGTCC
ACATGGGAGTCAGGTGTCATGGCTGCCCTGAGCTGGGAGGGAAGAAGGCTGACATTACATTT
AGTTTGCTCTCACTCCATCTGGCTAAGTGATCTTGAAATACCACCTCTCAGGTGAAGAACCG
TCAGGAATTCCCATCTCACAGGCTGTGGTGTAGATTAAGTAGACAAGGAATGTGAATAATGC
TTAGATCTTATTGATGACAGAGTGTATCCTAATGGTTTGTTCATTATATTACACTTTCAGTA
AAAAAA

FIGURE 92

MALMLSLVLSLLKLGSGQWQVFGPDKPVQALVGEDAAFSCFLSPKTNAEAMEVRFFRGQFSS
VVHLYRDGKDQPFMQMPQYQGR TKLVKDSIAEGRISLRLENITVLDAGLYGCRISSQSYQK
AIWELQVSALGSVPLISITGYVDRDIQLLCQSSGWFP RPPTAKWKGPQGDLSTDSRTNRDMH
GLFDVEISLTVQENAGSISCSMRHAHLSREVESRVQIGDTFFEPISWHLATKVLGILCCGLF
FGIVGLKIFFSKFQWKIQAE LDWRRKHGQAE LRDARKHAVEVT LDPETAHPKLCVSDLKTVT
HRKAPQEVPHSEKRFT RKS VVASQSFQAGKHYWEVDGGHNKRWRVGVC RDDVDRRKEYVTLS
PDHGYWVLRLNGEHL YFTLNPRFISVFPRT PPTKIGVFLDYECGTISFFNINDQSLIYTLTC
RFEGLLRPYIEYPSYNEQNGTPIVICPVTQESEKEASWQRASAI PETSNSSESSQATT PFLP
RGEM

Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 239-255

FIGURE 93

GCGATGGTGCGCCCGGTGGCGGTGGCGGCGGCGGTTGCGGAGGCTTCCTTGGTGGATTGCA
ACGAGGAGAAGATGACTGACCAACCGACTGGCTGAATGAATGAATGGCGGAGCCGAGCGCGC
CATGAGGAGCCTGCCGAGCCTGGGCGGCCTCGCCCTGTTGTGCTGCGCCGCCGCCGCCGCCG
CCGTGCGCTCAGCCGCCTCGGCGGGGAATGTCACCGGTGGCGGCGGGGCCGCGGGGCAGGTG
GACGCGTCGCCGGGCCCCGGGTTGCGGGGCGAGCCACAGCCACCCCTTCCCTAGGGCGACGGC
TCCACGGCCCAGGCCCCGAGGACCGGGCCCCCGCGCGCCACCGTCCACCGACCCCTGGCTG
CGACTTCTCCAGCCCAGTCCCCGGAGACCAACCCCTCTTTGGGCGACTGCTGGACCCTCTTCC
ACCACCTTTCAGGCGCCGCTCGGCCCCCTCGCCGACCACCCCTCCGGCGGCGGAACGCACTTC
GACCACCTCTCAGGCGCCGACCAGACCCGCGCCGACCACCCCTTTCGACGACCACTGGCCCCG
CGCCGACCACCCCTGTAGCGACCACCGTACCGGCGGCCACGACTCCCCGGACCCCGACCCCC
GATCTCCCCAGCAGCAGCAACAGCAGCGTCCTCCCCACCCACCTGCCACCGAGGCCCCCTC
TTCGCCTCCTCCAGAGTATGTATGTAACCTGCTCTGTGGTTGGAAGCCTGAATGTGAATCGCT
GCAACCAGACCACAGGGCAGTGTGAGTGTGCGCCAGGTTATCAGGGGCTTCACTGTGAAACC
TGCAAAGAGGGCTTTTACCTAAATTACACTTCTGGGCTCTGTCAGCCATGTGACTGTAGTCC
ACATGGAGCTCTCAGCATAACCGTGCAACAGGTAAGCAACAGAGGGTGGAACCTGAAGTTTATT
TTATTTTAGCAAGGGAAAAAAAAGGCTGCTACTCTCAAGGACCATACTGGTTTAAACAAAG
GAGGATGAGGGTCATAGATTTACAAAATATTTTATATACTTTTATTCTCTTACTTTATATGT
TATATTTAATGTCAGGATTTAAAAACATCTAATTTACTGATTTAGTTCTTCAAAAGCACTAG
AGTCGCCAATTTTTCTCTGGGATAATTTCTGTAAATTTTCATGGGAAAAAATTATTGAAGAAT
AAATCTGCTTTCTGGAAGGGCTTTCAGGCATGAAACCTGCTAGGAGGTTTAGAAATGTTCTT
ATGTTTATTAATATAACCATTTGGAGTTTGAGGAAATTTGTTGTTTGGTTTATTTTTCTCTCTA
ATCAAAATTCTACATTTGTTTCTTTGGACATCTAAAGCTTAACCTGGGGGTACCCTAATTTA
TTTAACTAGTGGTAAGTAGACTGGTTTTACTCTATTTACCAGTACATTTTTTGAGACCAAAAG
TAGATTAAGCAGGAATTATCTTTAAACTATTATGTTATTTGGAGGTAATTTAATCTAGTGGA
ATAATGTACTGTTATCTAAGCATTTCGCTTGTACTGCACTGAAAGTAATTATTCTTTGACCT
TATGTGAGGCACTTGGCTTTTTGTGGACCCCAAGTCAAAAAAAGTGAAGAGACAGTATTAAAT
AATGAAAAAATAATGACAGGTTATACTCAGTGTAACCTGGGTATAACCCAAGATCTGCTGC
CACTTACGAGCTGTGTTCCCTTGGGCAAGTAATTTCTTTCACTGAGCTTGTTTCTTCTCAAG
GTTGTTGTGAAGATTAAATGAGTTGATATATATAAAATGCCTAGCACATGTCACTCAATAAA
TTCTGGTTTGTTTTAAATTTCAAAGGAATATTATGGACTGAAATGAGAGAACATGTTTTAAGA
ACTTTTAGCTCCTTGACAAAGAAGTGCTTTATACTTTAGCACTAAATATTTTAAATGCTTTA
TAAATGATATTATACTGTTATGGAATATTGTATCATATTGTAGTTTATTAAAAATGTAGAAG
AGGCTGGGCGCGGTGGCTCACGCCTGTAATCCTAGCACTTTGGGAGGCCAAGGCGGGTGGAT
CACTTGAGGCCAGGAGTTCTAGATGAGCCTGGCCAGCACAGTGAAACCCCGTCTCTACTAAA
AATACAAACAAATTAGCTGGGCGTGGTGGCACACACCTGTAGTCCCAGCTACTCGGGAGGCT
GAGGCAGGAGAATCGGTTGAACCCGGGAGGTGGAGGTTGCAGTGAGCTGAGATCGCGCCACT
GCACTCCAGCCTGGTGAGAGAGGGAGACTCTGTCTTAAAAAATAAAAAAAAAAAAAAAAAA

FIGURE 94

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64952

><subunit 1 of 1, 258 aa, 1 stop

><MW: 25716, pI: 8.13, NX(S/T): 5

MRSLSLGLGLALLCCAAAAA AVASAASAGNVTGGGGAAGQVDASPGPGLRGEPSHPFPRATA
PTAQAPRTGPPRATVHRPLAATSPAQSPETTPPLWATAGPSSTTFQAPLGPSPPTTPPAAERTS
TTSQAPTRPAPTTLSTTTGPAPTTPVATTVPAPTTPRTPTDLPSSSNSSVLPTPPATEAPS
SPPPEYVCNCSVVGSLNVNRCNQTTGQCECRPGYQGLHCETCKEGFYLNYSGLCQPCDCSP
HGALSIPCNR

Important features of the protein:

Signal peptide:

amino acids 1-25

N-glycosylation sites.

amino acids 30-33, 172-175, 195-198, 208-211, 235-238

EGF-like domain cysteine pattern signature.

amino acids 214-226.

FIGURE 95

TGCGGCGCAGTGTAGACCTGGGAGGATGGGCGGCCTGCTGCTGGCTGCTTTTCTGGCTTTGG
TCTCGGTGCCCAGGGCCCAGGCCGTGTGGTTGGGAAGACTGGACCCTGAGCAGCTTCTTGGG
CCCTGGTACGTGCTTGCGGTGGCCTCCCGGGAAAAGGGCTTTGCCATGGAGAAGGACATGAA
GAACGTCGTGGGGGTGGTGGTGACCCTCACTCCAGAAAACAACCTGCGGACGCTGTCCTCTC
AGCACGGGCTGGGAGGGTGTGACCAGAGTGTGATGGACCTGATAAAGCGAAACTCCGGATGG
GTGTTTGAGAATCCCTCAATAGGCGTGCTGGAGCTCTGGGTGCTGGCCACCAACTTCAGAGA
CTATGCCATCATCTTCACTCAGCTGGAGTTCGGGGACGAGCCCTTCAACACCGTGGAGCTGT
ACAGTCTGACGGAGACAGCCAGCCAGGAGGCCATGGGGCTCTTCACCAAGTGGAGCAGGAGC
CTGGGCTTCCTGTCACAGTAGCAGGCCCAGCTGCAGAAGGACCTCACCTGTGCTCACAAGAT
CCTTCTGTGAGTGCTGCGTCCCCAGTAGGGATGGCGCCACAGGGTCCTGTGACCTCGGCCA
GTGTCCACCCACCTCGCTCAGCGGCTCCCGGGGCCAGCACCAGCTCAGAATAAAGCGATTC
CACAGCA

FIGURE 96

MGGLLLAAFLALVSVPRQAQAVWLGRDLPEQLLGPWYVLAVASREKGFAMEKDMKNVVGVVVT
LTPENNLRTLSSQHGLGGCDQSVMDLIKRN SGWVFENPSIGVLELWVLATNFRDYAII FTQL
EFGDEPFNTVELYSLTETASQEAMGLFTKWSRSLGFLSQ

Signal peptide:
amino acids 1-20

FIGURE 97

AACAGACGTTCCCTCGCGGCCCTGGCACCTCTAACCCCAGACATGCTGCTGCTGCTGCTGCC
CCTGCTCTGGGGGAGGGAGAGGGCGGAAGGACAGACAAGTAAACTGCTGACGATGCAGAGTT
CCGTGACGGTGCAGGAAGGCCTGTGTGTCCATGTGCCCTGCTCCTTCTCCTACCCCTCGCAT
GGCTGGATTTACCCTGGCCCAGTAGTTCATGGCTACTGGTTCCGGGAAGGGGCCAATACAGA
CCAGGATGCTCCAGTGGCCACAAACAACCCAGCTCGGGCAGTGTGGGAGGAGACTCGGGACC
GATTCCACCTCCTTGGGGACCCACATACCAAGAATTGCACCCTGAGCATCAGAGATGCCAGA
AGAAGTGATGCGGGGAGATACTTCTTTCGTATGGAGAAAGGAAGTATAAAATGGAATTATAA
ACATCACCGGCTCTCTGTGAATGTGACAGCCTTGACCCACAGGCCCAACATCCTCATCCCAG
GCACCCTGGAGTCCGGCTGCCCCCAGAATCTGACCTGCTCTGTGCCCTGGGCCTGTGAGCAG
GGGACACCCCTATGATCTCCTGGATAGGGACCTCCGTGTCCCCCTGGACCCCTCCACCAC
CCGCTCCTCGGTGCTCACCCCTCATCCACAGCCCCAGGACCATGGCACCAGCCTCACCTGTC
AGGTGACCTTCCCTGGGGCCAGCGTGACCACGAACAAGACCGTCCATCTCAACGTGTCCTAC
CCGCCTCAGAACTTGACCATGACTGTCTTCCAAGGAGACGGCACAGTATCCACAGTCTTGGG
AAATGGCTCATCTCTGTCACTCCAGAGGGCCAGTCTCTGCGCCTGGTCTGTGCAGTTGATG
CAGTTGACAGCAATCCCCCTGCCAGGCTGAGCCTGAGCTGGAGAGGCCTGACCCTGTGCCCC
TCACAGCCCTCAAACCCGGGGGTGCTGGAGCTGCCTTGGGTGCACCTGAGGGATGCAGCTGA
ATTCACCTGCAGAGCTCAGAACCCTCTCGGCTCTCAGCAGGTCTACCTGAACGTCTCCCTGC
AGAGCAAAGCCACATCAGGAGTGACTCAGGGGGTGGTCCGGGGGAGCTGGAGCCACAGCCCTG
GTCTTCCTGTCCTTCTGCGTCATCTTCGTTGTAGTGAGGTCCTGCAGGAAGAAATCGGCAAG
GCCAGCAGCGGGCGTGGGAGATACGGGCATAGAGGATGCAAACGCTGTCAGGGGTTTCAGCCT
CTCAGGGGCCCCTGACTGAACCTTGGGCAGAAGACAGTCCCCCAGACCAGCCTCCCCCAGCT
TCTGCCCCGCTCCTCAGTGGGGGAAGGAGAGCTCCAGTATGCATCCCTCAGCTTCCAGATGGT
GAAGCCTTGGGACTCGCGGGGACAGGAGGCCACTGACACCGAGTACTCGGAGATCAAGATCC
ACAGATGAGAACTGCAGAGACTCACCCCTGATTGAGGGATCACAGCCCCTCCAGGCAAGGGA
GAAGTCAGAGGCTGATTCTTGTAGAATTAACAGCCCTCAACGTGATGAGCTATGATAACACT
ATGAATTATGTGCAGAGTGAAAAGCACACAGGCTTTAGAGTCAAAGTATCTCAAACCTGAAT
CCACACTGTGCCCTCCCTTTTATTTTTTTAACTAAAAGACAGACAAATTCCTA

FIGURE 98

MLLLLLPLLWGRERAEGQTSKLLTMQSSVTVQEGLCVHVPCSFSPSHGWIYPGPVVHGYWF
REGANTDQDAPVATNNPARAVWEETRDRFHLLGDPHTKNCTLSIRDARRSDAGRYFFRMEKG
SIKWNKYKHHRLSVNVTALTHRPNILIPGTLESGCPQNLTCVWPWACEQGTPPMISWIGTSVS
PLDPSTTRSSVLTLLIPQPQDHGTS LTCQVTFPGASVTTNKT VHLNVSYPQNL TMTVFQGDG
TVSTVLGNGSSLSLPEGQSLRLVCAVDAVDSNPPARLSLSWRGLTLCPSQPSNPGVLELPWV
HLRDAAEFTCRAQNPLGSQQVYLNVSLSQSKATSGVTQGVVGGAGATALVFLSFCVIFVVVRS
CRKKSARPAAGVGD TGIEDANAVRG SASQG PLTEPWAEDSPPDQPPASARSSVGE GELQYA
SLSFQMVKPWDSRGQEATDTEYSEIKIHR

Signal peptide:

amino acids 1-15

Transmembrane domain:

amino acids 351-370

FIGURE 99

GACGCCCAGTGACCTGCCGAGGTCGGCAGCACAGAGCTCTGGAGATGAAGACCCTGTTCTCTG
GGTGTACGCTCGGCCTGGCCGCTGCCCTGTCCTTCACCCTGGAGGAGGAGGATATCACAGG
GACCTGGTACGTGAAGGCCATGGTGGTCGATAAGGACTTTCGGGAGGACAGGAGGCCCCAGGA
AGGTGTCCCCAGTGAAGGTGACAGCCCTGGGCGGTGGGAAGTTGGAAGCCACGTTACCTTC
ATGAGGGAGGATCGGTGCATCCAGAAGAAAATCCTGATGCGGAAGACGGAGGAGCCTGGCAA
ATACAGCGCCTATGGGGGCAGGAAGCTCATGTACCTGCAGGAGCTGCCCAGGAGGGACCACT
ACATCTTTTACTGCAAAGACCAGCACCATGGGGGCCTGCTCCACATGGGAAAGCTTGTGGGT
AGGAATTCTGATACCAACCGGGAGGCCCTGGAAGAATTTAAGAAATTGGTGCAGCGCAAGGG
ACTCTCGGAGGAGGACATTTTCACGCCCCTGCAGACGGGAAGCTGCGTTCCCGAACACTAGG
CAGCCCCCGGGTCTGCACCTCCAGAGCCCACCCTACCACCAGACACAGAGCCCGGACCACCT
GGACCTACCCTCCAGCCATGACCCTTCCCTGCTCCCACCCACCTGACTCCAAATAAAGTCCT
TTTCCCCCAA